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**ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND  
RELATED MATTERS.**

Hearing held in Court Room 20  
Court House  
361 University Avenue  
Toronto, Ontario

**The Honourable Mr. Justice S.G.M. Grange**

Commissioner

**P.S.A. Lamek, Q.C.**

Counsel

**E.A. Cronk**

Associate Counsel

**Thomas Millar**

Administrator

Transcript of evidence  
for

June 23rd, 1983

VOLUME 3

**OFFICIAL COURT REPORTERS**

Angus, Stonehouse & Co. Ltd.,  
14 Carlton Street, 7th Floor,  
Toronto, Ontario M5B 1J2

595-1065







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Hearing held in Court Room 20,  
Court House, 361 University  
Avenue, Toronto, Ontario, on  
Thursday the 23rd day of June,  
1983.

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner  
THOMAS MILLAR - Administrator  
MURRAY R. ELLIOTT - Registrar

APPEARANCES:

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L. CECCHETTO )	General of Ontario (Crown
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I.G. SCOTT, Q.C.)	Counsel for The Hospital for
I. J. ROLAND )	Sick Children
D. YOUNG	Counsel for The Metropolitan
	Toronto Police
K. CHOWN	Counsel for numerous Doctors
	at The Hospital for Sick
	Children
F. KITELY	Counsel for the Registered
	Nurses' Association of
	Ontario and 35 Registered
	Nurses at The Hospital for
	Sick Children







APPEARANCES: (Continued)

W.A. BOGART	Counsel for Susan Nelles - Nurse
G.R. STRATHY) P. RAE )	Counsel for Phyllis Trayner - Nurse
C. BUHR	Counsel for Sui Scott - Nurse
J.A. OLAH	Counsel for Janet Brownless (Vereecken) R.N.A.
N. GOODMAN	Counsel for Mrs. Christie - R.N.A.
M. MANNING, Q.C.) S. LABOW )	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, and Mr. & Mrs. Lutes (parents of deceased children)
F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo)
W.T. TOBIAS	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)





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---Upon commencing at 10:00 a.m.

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THE COMMISSIONER: Yes, Mr. Strathy,

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GEORGE CIMBURA, Resumed

5

CROSS-EXAMINATION BY MR. STRATHY:

6

Q. Mr. Cimbura, as I understand it, digoxin as a drug has been around for many, many years, is that so?

7

8

9

A. For many years, that's right, sir.

10

11

Q. And it has been used in the treatment of heart disease for many years?

12

A. That's right, sir.

13

14

Q. As I understand it, it is a derivative of the foxglove plant, is that so?

15

16

A. Yes, it can come from that source, as well as, I believe, some other plant materials.

17

18

Q. It can also be produced or synthesized without resort to the plant itself?

19

A. Possibly, yes.

20

Q. Are you aware of that or not?

21

A. No, I haven't really reviewed the literature on the synthesis of digoxin.

22

23

Q. I have seen digoxin referred to as a cardiac glycoside. Are you familiar with

24

25

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in 2023 with funding from  
University of Toronto





1

2

that term?

3

A. Yes, sir.

4

5

Q. And just briefly can you assist us as to what a cardiac glycoside is?

6

7

A. Well, the cardiac of course is a reference to the heart and I would presume reference to the action of the drug in the heart.

8

9

Q. That it acts upon the heart, is that right?

10

A. That's right.

11

Q. And glycoside?

12

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14

A. And glycoside is a chemical term which applies to a certain configuration, chemical configuration of naturally occurring materials.

15

16

17

Q. And would I be correct in understanding that glycoside has a reference to sugar or sugar as a component?

18

19

20

A. Digoxin and some of the derivatives have sugar molecules attached to that, that's right.

21

22

Q. So that a digoxin molecule has a sugar attached to it?

23

24

25

A. Actually, the digoxin molecule has, as I recall it, three molecules and sugar called





1  
2 digitoxose.

3 Q. Digitoxose?

4 A. Digitoxose, that's right.

5 Q. You made reference in your  
6 evidence yesterday to something called digitoxin.  
7 Would you mind briefly explaining the difference  
8 between digoxin and digitoxin?

9 A. Yes, digitoxin is a cardiac  
10 glycoside and it has a somewhat chemical configura-  
11 tion. It is very similar chemically to digoxin  
12 but there is a difference in the chemical composition.  
13 It has some differences, pharmacological differences  
as well.

14 Q. Is it digitoxin also used in  
15 the treatment of heart disease?

16 A. It has been used, to what  
17 extent it is used right now, if at all, I think  
18 it would be a question to be answered by a medical  
practitioner.

19 Q. Rather than by yourself?

20 A. Pardon me?

21 Q. Rather than by yourself?

22 A. Yes, the current treatment with drugs  
23 I feel should be a question for a physician.

24 Q. Fair enough. Now, Mr. Cimbura,  
25







1  
2 I understand that while digoxin has been used in the  
3 treatment of heart disease for many years, it is  
4 only in relatively recent years that it has been  
5 used, or that it has been possibly to use this RIA  
6 technique to detect digoxin, is that so?

7 A. Yes, I would agree with that.  
8 If I may generalize, because there have been a  
9 number, or many publications on the subject in the  
10 scientific literature but it would appear to me that  
11 the RIA analyses started to be reported in the early  
12 1970s.

13 Q. So, since the early 1970s,  
14 would it be fair to say that is when in effect the  
15 RIA method was developed insofar as digoxin is  
16 concerned?

17 A. Has been developed, has been  
18 applied to the analyses for digoxin and various  
19 modifications right from the early stages to the  
20 later stages. For example, the early stages a  
21 tritiated label was used as opposed to an iodinated  
22 label and some other modifications.

23 Q. I am not at this point at least  
24 too concerned about the precise modifications or  
25 details of the test, but as I understand it, sir,  
I'm instructed that it was in about 1969 or 1970







1  
2 that the particular assay for the detection of  
3 digoxin was developed. Would that be consistent  
4 with your knowledge?

5 A. Well, as I have mentioned  
6 previously, my recollection is early seventies, it  
7 could be late sixties, that's right.

8 Q. I also understand that the  
9 primary use for the RIA method when it was developed  
10 was for the detection of digoxin in a therapeutic  
11 setting in the hospital setting, is that so?

12 A. It sounds reasonable to me.

13 Q. That would be for the purpose  
14 of monitoring patients who are on digoxin so that  
15 you would know the level of digoxin in their systems.

16 A. That's right.

17 Q. And, as I understand it, the  
18 purpose of it is so that you know or the doctor  
19 knows whether the patient is getting a sufficient  
20 dose or, indeed, whether the patient is getting an  
21 excessive dose. Is that so?

22 A. Yes, it's a guideline to a  
23 physician to monitor the treatment.

24 Q. For those reasons to know  
25 whether the patient is getting enough digoxin or  
too much digoxin.





1  
2  
3 A. Well, yes. Generally speaking  
4 if the level is within the accepted normal range  
5 then generally there is no concern. If it is about  
6 that range, that requires usually an investigation  
and possible adjustments to various aspects.

7 Q. Or presumably if you were  
8 administering digoxin to the patient and there's  
9 not enough digoxin showing up on the tests, you would  
10 want to do something about your digoxin administration?

11 A. Possibly, yes.

12 Q. And for the purpose of doing  
13 these tests, as I understand it, the hospitals  
14 acquire, or the hospital Toxicology Departments  
15 acquire these kits that you referred to for the  
detection of digoxin by RIA?

16 A. Well, I'm not sure whether  
17 they acquire the kits I referred to specifically,  
18 but some form of RIA assays.

19 Q. No, I didn't mean the very  
20 same kit you used, I just mean kits are commercially  
available and hospitals would acquire them.

21 A. They may acquire them, that's  
22 right.

23 Q. Now, you mentioned that just  
24 a moment ago about the monitoring of digoxin and I  
25







1  
2 gather that there is a danger in any patient  
3 receiving digoxin, that he or she may receive too  
4 much digoxin in what is known as a toxic amount.  
5 Is that accurate?

6 A. Well, a person may take or,  
7 I suppose, receive by accident an excessive amount.

8 Q. Well, indeed, leaving apart  
9 accidental, I gather that in the case of patients  
10 receiving digoxin on a therapeutic basis, there is  
11 a distinct danger that over the course of the  
12 administration they may have received too much and  
13 in effect have toxic levels of digoxin in their  
blood, is that so?

14 A. Well, this digoxin therapy  
15 does require careful monitoring because of the  
16 potent nature of the drug.

17 Q. Yes, you mentioned that yester-  
18 day. All I'm asking you is there a danger that  
19 the patient may in effect receive toxic doses while  
under therapeutic maintenance of digoxin?

20 A. Well, under some clinical  
21 conditions the levels may become elevated in the  
22 blood, in the plasma, yes.

23 Q. You are well aware with the  
24 term toxic?  
25







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A. Yes, that's right.

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Q. And I'm asking you, is there a  
danger that the levels can become toxic?

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A. Yes, the level may become  
elevated and this may indicate toxicity, may  
produce toxicity, that's right, depending on what  
the elevation is and any other circumstances.

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Q And just to assist us with the matter of knowing, as I understand it when a person on digoxin has reached a toxic state it is referred to as digitoxin, is that right, or are you familiar with that?

A I am not familiar specifically with that term.

Q You mentioned in relation to this toxicity problem the potency of the drug, but would I also be correct in understanding that toxicity may be a problem because the borderline between what a therapeutic dose is and what a toxic dose is is a relatively fine line?

A There is an overlap between the therapeutic and the toxic ranges.

Q So I shouldn't have called it a line I should have indicated that there is some merger of the two?

A There is some overlap between the two, yes.

Q And for that reason toxicity may well be a problem?

A As well as the potency, as well the interpretation of the level may be a problem with respect to toxicity because of the overlap.







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Q. Not simply the interpretation but the fact, the effect on the patient may be toxic as opposed to therapeutic because of this overlap, would you agree with that?

A. Would you say that again, I am not sure I heard.

Q. The fact that a patient rather than being therapeutic may well be toxic because of this very overlap which you have referred to, would you agree with that?

A. To some extent, yes.

Q. And you were assisting us yesterday with respect to the therapeutic doses of digoxin, and I appreciate this may not be your particular area, but you mentioned two levels, one with respect to adults and one with respect to children under six months, or infants under six months. Can you assist us as to the dose for infants in the six month to two year range that I think was your upper limit for infants, can you assist us as to what the therapeutic dose would be under those circumstances?

I am sorry, you weren't talking in terms of doses in the sense of how much is injected, but what the level should be, I stand corrected. Can





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you assist us in that area?

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A. No, I cannot assist you, which

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area?

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Q. I'm sorry.

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A. What is your question now, please?

7

Q. You were assisting us on the

8

therapeutic levels, you mentioned the adult therapeutic level and you mentioned the therapeutic level

9

for infants under six months.

10

A. That's right.

11

Q. And I am asking you if you are

12

aware of what the therapeutic level is for infants

13

between six months and two years of age, are you able

14

to assist us in that regard? If you are not able to assist us by all means say so.

15

A. I would prefer not to answer

16

that

17

Q. Very well. Just one question

18

on these levels. You mentioned obviously that the

19

level, therapeutic level for infants or babies is

20

apparently higher than the therapeutic level for

21

adults. Do I take it from that that infants are

22

better able to tolerate digoxin than adults, would you agree with that statement?

23

A. There have been a number of

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reports and literature offering various reasons for  
this.

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Q Well, I am not asking you at  
this point the reasons, I am simply asking you  
whether you agree with that, sir.

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A Okay, I would prefer again not  
to answer this question because there appears to be  
different points of view. Perhaps a paediatrician,  
or a specialist in paediatrics would be better  
qualified to answer that.

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Q Fair enough. You gave evidence  
yesterday as to your, what I will call relative  
inexperience with digoxin and your relative  
inexperience in the Centre with digoxin. Am I correct,  
sir, that when you and the Centre were first approached  
by the Metropolitan Toronto Police in March of 1981  
in respect of the investigation that was going on at  
that time, you expressed a great reluctance to become  
involved in the analysis of the samples that were  
submitted to you, for the very reason of your  
inexperience, is that so?

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A Yes. Essentially that was it, we  
had no specific experience with digoxin analysis, plus  
there was the other complicating factor, some of the,  
or many of the items received, specimens received were





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very unusual and for that reason we were reluctant to become involved if there was someone else better qualified for this purpose.

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Q. So in fact when the police first knocked on your door you sent them away and suggested that they try elsewhere first, is that so?

6

7

8

A. They tried, and I tried as well to find some other source that may be more qualified.

9

10

11

Q. And ultimately I take it your efforts and their efforts came to naught and they came back to the Centre, is that so?

12

13

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A. As far as I recall, yes, there was no other agency or person and because of the seriousness of the investigation we agreed to become involved providing we were given some time to do the necessary preliminary research that I felt was required.

17

18

Q. This is the research that you referred to yesterday?

19

20

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A. I referred to some research.

Q. You mentioned your reluctance in view of, I think I am repeating your words, the unique nature of some of the specimens submitted to you. I gather among other things -- I am sorry, unusual nature of the specimens submitted to you, and I





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believe among other things you were submitted tissue samples which had been stored in effect in formaldehyde or some other preservative for a number of months, is that one of the things you were asked to analyze?

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A. Yes, it was diffused, sort of fixed in various chemicals.

8

Q. The expression is "fixed"?

9

A. That is the term I have become familiar with. In a sense these tissues that are contained in chemicals, that's right, in liquid chemicals.

12

13

14

Q. These tissues as I understand it were taken at the time of autopsy and put in a, fixed in a solution, is that right?

15

16

17

18

19

A. Well, I wasn't there when the tissue was taken, when it was put into the chemical preservative, but this is I understand some time after the autopsy they were placed in that, that's right.

20

21

22

Q. That is your understanding when these things were given to you was that they were taken at or about the time of autopsy and preserved?

23

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A. At some time placed into the preservative, that's right.







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Q. Now, another thing which you received which I take it you considered unusual was tissue from infants who had been exhumed some considerable time after death?

A. That is correct, sir.

Q. And both of those things, the fixed tissues and the tissues which came from exhumed bodies, in your experience and as far as you could tell in the literature were unique or unusual?

A. That is correct, sir. Unusual with respect to analyzing them and interpreting possible results.

Q. Well, they presented an unusual problem also in the sense that there had not been research, or reports, in the literature, at least to your knowledge, when you were given the task?

A. That is correct.

Q. I would like to ask you some questions, Mr. Cimbura, about the reaction of digoxin with other things insofar as, I think perhaps I should restate this. The reaction of the RIA method of analysis with other things, things other than digoxin.





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And you firstly mentioned what you referred to as the metabolites of digoxin which in lay terms, as I understand it, are the breakdown products of digoxin. Is that fair enough?

A. Breakdown products by the body, that is right.

Q. And you indicated that the RIA test may show up not only digoxin but also its metabolites?

A. That is right.

Q. Do I understand that in the normal course of things, in the normal functioning of the human body, these metabolites will eventually be excreted through the body over a period of some days?

A. This is in general the purpose of metabolism is to facilitate the elimination of drugs from the body.

Q. And in fact not only the metabolites but also the digoxin eventually leave the body?

A. That is right.

Q. Through the process of elimination through urine. Is that accurate?

A. That is right.

Q. You mentioned, sir, a problem of







1  
2 renal failure yesterday in your evidence, and as I  
3 understand, renal failure to be kidney failure. Is  
4 that so?

5 A. That is right. Form of impair-  
6 ment of kidney functions.

7 Q. And you indicated, sir, that in  
8 cases in which there is renal failure there may be a  
9 build-up of these metabolites in the body because the  
10 kidney is not able to excrete them as efficiently as  
it might otherwise do?

11 A. That is correct.

12 Q. And I take it from that that one  
13 of the questions we would want to know when we are  
14 looking at a particular, in this case, infant treated  
15 with digoxin or otherwise, is whether in fact there  
has been renal failure. Would you agree with that?

16 A. Renal impairment or renal  
17 failure, that is correct, sir.

18 Q. Does your knowledge, sir, of  
19 pharmacology extend to knowledge of a relationship  
20 between heart failure and renal failure?

21 A. Well, that is really a medical  
22 rather than pharmacological terms.

23 Q. Let me just put a question to  
24 you then and if you are not able to assist us, please  
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say so.

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I am instructed, sir, there is in many cases a relationship between heart failure, ~~construc-~~ *Congestive* ~~tive~~ heart failure, and renal failure, because the heart is not able to pump blood to the kidneys sufficiently efficiently to keep the kidneys going as they should.

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Can you agree with that statement?

9

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A. I would not comment on that. I think this is a medical specialist ...

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12

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Q. All right. Fair enough. Maybe you can help me with this, though, as a pharmacologist. Do I understand correctly that when there is renal failure, one of the things that you treat renal failure with is what is called a diuretic? That is surely a pharmacological question.

16

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A. I am familiar with the term, but again I feel that there will be medical people who will be more qualified than I am to answer that question.

20

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Q. Well, you are familiar with the term, I am sure, diuretic?

A. That is right.

Q. And is a diuretic not used in the treatment of kidney failure to help the kidneys





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void more efficiently?

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A. I think this is in a medical jurisdiction.

4

5

Q. You can't answer that question fairly today. Is that what you are saying?

6

7

A. I would prefer not to comment on aspects dealing with medical treatment.

8

9

Q. All right. I notice the second thing you mentioned might react with the RIA test was other drugs and I understood you to be referring to other drugs in the digoxin family, other cardiac glycosides; is that right?

10

11

12

A. Yes. As I recall it, I used some examples, that is right.

13

14

Q. You mentioned lanatoside C, digitoxin and deslanoside?

15

16

A. That is right. I believe I mentioned those, yes.

17

18

Q. And to assist us, sir, are those all cardiac glycosides?

19

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A. They are - I am trying to go over the chemical structure of those two.

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Q. Well, I can --

23

A. Digoxin, compounds similar to digoxin and --

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Q. Are they also used in the treatment of heart disease?

A. They have been used. I am not sure whether they are still used but they have been used at some time, that is right.

Q. All right. In any case, sir, in the case of those drugs if we are using RIA method we should be aware of the fact that that method may show up digoxin as well as those other drugs without distinguishing between them?

A. That is correct, sir.

Q. Now the next area I would like to ask you about in terms of the RIA test and other things are the relationship of that test to other drugs, and I think the question of cocaine was raised yesterday, and of course you said it wouldn't detect cocaine. Do you recall that?

A. I said I would not expect to - that cocaine would react to the RIA test for digoxin.

Q. All right. That is fair enough. But let me ask you this, sir. Are you aware of reasonably current research that indicates that the simultaneous treatment of patients with digoxin and certain other drugs may result in a cross-reaction with digoxin antiserum which gives apparently toxic





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digoxin levels.

Do you understand my question?

A. Would you repeat that again,  
please?

Q. Certainly.

MR. LAMEK: Mr. Commissioner, I  
wonder, too, if Mr. Strathy could be a little more  
specific rather than "relatively recent research"  
and "other drugs". It might be helpful to Mr.  
Cimbura.

MR. STRATHY: I will come to those in  
short order, Mr. Commissioner. I do have specifics  
I would like to put --

MR. LAMEK: Why not come to them  
now so that Mr. Cimbura may recognize the reference  
if he knows of it?

THE COMMISSIONER: Yes. I will allow  
the question the way it is. It might help - there is  
no question it might help if you give the nature of  
the research, where it is, the name of it, it might  
bring --

MR. STRATHY: I can come to that I  
suppose, and I will do that.

THE COMMISSIONER: All right.

MR. STRATHY: I will mention specific







1  
2 drugs, I don't think there is any point at this stage  
3 at least in getting on to the specific publications,  
4 but I will mention the drugs.

5 Q. Let me phrase my general  
6 question, sir, first, and that is this: are you aware  
7 of recent research that indicates that in the  
8 simultaneous treatment of patients with digoxin and  
9 certain other drugs there may be a cross-reactivity  
10 or a cross-reaction with digoxin <sup>bother</sup> ~~antiserum~~ which gives  
11 apparently toxic digoxin levels when in fact the  
12 levels are at therapeutic? So the effect of that is  
13 that you have inflated digoxin levels.

14 Now that was my general question, sir.  
15 Let me make it specific and refer to some specific  
16 drugs. Firstly, furosemide, f-u-r-o-s-e-m-i-d-e,  
17 which I understand is sometimes called lasix,  
18 l-a-s-i-x, and secondly --

19 THE COMMISSIONER: How is that spelled  
20 again?

21 MR. STRATHY: Excuse me, l-a-s-i-x.

22 THE COMMISSIONER: And it is  
23 pronounced you say?

24 MR. STRATHY: I believe it is  
25 pronounced lasix.

- - - -





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Q. Secondly, Mr. Cimbura,

spironolactone, s-p-i-r-o-n-o-l-a-c-t-o-n-e, which,  
as I understand it, is also referred to as aldactone,  
a-l-d-a-c-t-o-n-e.

Now, let me give you my question in  
perhaps three parts.

Firstly, are you familiar with  
furosemide and spironolactone? Are you familiar  
with it?

A. Yes, I'm familiar with that,  
with the chemical, with the drugs, yes.

Q. And, secondly, sir, do you  
recognize those as diuretics? Without saying  
whether you know what diuretics are used for, do  
you recognize them as being labelled diuretics  
pharmacologically?

A. One of them, yes. I don't  
recall the other one.

Q. Which one do you recognize as  
a diuretic?

A. Lasix.

Q. That's furosemide?

A. That's right.

Q. But you're not sure whether  
aldactone or spironolactone are diuretics?





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A. I don't recall right now their mode of action. They may be, but I don't recall it.

Q. All right. Then my next question, sir, is, are you aware of research which indicates that there may be a cross reaction between the two drugs that I've just mentioned and digoxin which gives elevated digoxin levels under RIA testing? Are you aware of that research?

A. That gives elevated?

Q. Yes.

A. I am familiar with the possibility with the drug spironolactone with respect to reported apparent occurrences of elevated digoxin levels analyzed by RIA. The way I understand it is that this depends on the cross reactivity of a particular antibody that is being used.

Just so I'm aware though, you are aware of a cross reactivity between spironolactone and digoxin using the RIA method? You are aware of that?

A. Between an apparent cross reactivity with some RIA antibodies.

Q. Well, the effect of that apparent cross reactivity I think you will agree with me is to give elevated digoxin levels?







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2

A. If it happens, that is right,

3

yes.

4

Q. That's what you, when you are

5

reading the levels, they appear to be elevated and

6

the apparent reason they are elevated is because

7

of the presence of this spironolactone?

8

A. That's right.

9

Q. So that a patient being treated

10

simultaneously with digoxin for one reason and,

11

let us say, spironolactone for renal failure might

12

well show up elevated digoxin levels on RIA testing.

13

Is that so?

A. With some RIA reagents, yes.

14

Q. Using some RIA kits, is that

15

right?

16

A. That's not necessarily all,

17

that's right. I should add if I may, since I think

18

it is relevant, that the drug, because of this,

19

which I was aware of, the drug was one of the drugs

20

that was tested for separation in our laboratory

from the drug digoxin on the HPLC.

21

Q. So, this cross reactivity was

22

something that you were aware of, sir, when you did

23

your tests?

24

A. When we designed and evaluated

25





1

2

our procedure, that's right, yes.

3

Q. Were you aware -- I'm sorry.

4

A. If I may still add one more

5

which I believe is pertinent information.

6

Q. I'm sorry.

7

A. In my research I've had occasion

8

to use our RIA test on one infant that was receiving  
the therapy with this drug.

9

Q. With which drug, excuse me?

10

A. With the spironolactone.

11

Q. I see.

12

A. And with not digoxin and, in

13

this instance, our RIA test was negative.

14

Q. So, when there was no digoxin

15

being administered spironolactone did not show up  
in the RIA test?

16

A. The spironolactone was

17

administered but there was no apparent digoxin  
reading.

18

19

Q. In your test, sir, did you test

20

for this cross reactivity? Did you observe this

21

cross reactivity between digoxin and spironolactone?

22

A. We have tested, as I mentioned,

23

on the HPLC to make sure there is a separation.

24

Q. I understand that, but I'm not

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D5 talking about that, I'm talking about on the RIA test. Did you observe this apparent increase effect in your own RIA test?

A. Oh, no, I didn't. As I mentioned, I have analyzed one specimen of blood from an infant who was on spironolactone therapy.

Q. With digoxin?

A. No, without digoxin.

Q. Right. Let me be more specific then. I'm asking you, you have mentioned that you are familiar with the research in this area?

A. Yes.

Q. I'm asking you whether your own observations in your own laboratory bore this research out? Did you find an interrelationship or a cross reactivity between digoxin and spironolactone, or did you look at it at all; if you didn't look at it at all, then we can move to something else?

A. Well, I have explained I thought clearly that I have looked at it and I was aware of it.

Q. But did you look at it in the laboratory sense, in the sense of taking a sample of one or more children who had been administered digoxin and spironolactone and did you observe in





1

2

that case elevated, apparently elevated digoxin  
levels?

3

4

A. I have studied one case of an  
infant who was on spironolactone.

5

6

Q. But not digoxin?

7

A. But not digoxin.

8

Q. But my question --

9

A. This was the purpose of it  
because if the child would have been on digoxin  
I wouldn't have known whether the RIA gives an  
elevated result or not.

10

11

12

Q. I understand that, sir, but I  
don't think my question is too difficult to follow.  
I'm asking you whether you looked at them side by  
side in one infant being administered both digoxin  
and spironolactone. Did you make observations of  
that situation?

14

15

16

17

A. I would have to go through my  
research notes on that before I could answer that.

18

19

Q. All right, would you mind doing  
that?

20

21

A. Yes.

22

Q. So that when you come the next  
day you can answer that. I'm sure that Mr. Lamek  
will make a note of that.

23

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D7

A. Sure. If I may, I'll mark it down.

Q. I'm sure Mr. Lamek will, you don't need to.

Now, you have told us, sir, that you were aware of this spironolactone cross-reactivity and that you made allowances for it in your HPLC testing?

A. That's correct, sir.

Q. My question is, were you aware of the furosemide or lasix reactivity at the time you were doing these tests?

A. I recall reading literature suggesting elevation I believe, possible elevation of digoxin levels. I'm not really, I haven't formed a conclusion that this was a potential serious problem, as I recall it.

Q. All right then.

A. With this particular drug.

Q. May I take it correctly then that in your HPLC analysis you did not make a particular run or test for furosemide then, is that accurate?

A. Yes, as I recall it, that's right.







1  
2  
3 Q. Now, I'd like to turn to two  
4 other drugs, sir, again falling within my same  
5 general question I'm going to try and be specific  
6 for you - in fact, four other drugs. They are,  
7 firstly, quinidine, q-u-i-n-i-d-i-n-e, verapamil,  
8 v-e-r-a-p-a-m-i-l.

9 THE COMMISSIONER: Again, Mr. Strathy.

10 MR. STRATHY: I'm sorry. The first  
11 was quinidine, q-u-i-n-i-d-i-n-e, secondly verapamil,  
12 v-e-r-a-p-a-m-i-l.

13 THE COMMISSIONER: It's starts with  
14 a "v", does it?

15 MR. STRATHY: Yes. Thirdly,  
16 nifedipine, n-i-f-e-d-i-p-i-n-e and, fourthly,  
17 amiodarone, a-m-i-o-d-a-r-o-n-e. I make no warranty  
18 that I have pronounced them correctly, but I think  
19 I spelled them correctly.

20 Q. Now, I am instructed, Mr. Cimbura,  
21 that those drugs are heart drugs, or drugs that are  
22 used in the treatment of heart patients. Do you  
23 recognize the drugs that I have just mentioned?

24 A. Would you give them to me again,  
25 please.

Q. Quinidine, verapamil, nifedipine ---

A. What is the third one?





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Q. Nifedipine, n-i-f-e-d-i-p-i-n-e.

3

A. N-i-f-e-d-i-p-i-n-e.

4

Q. And, lastly, amiodarone,

5

a-m-i-o-d-a-r-o-n-e.

6

Now, let's just take this one step

7

at a time, please.

8

Firstly, without telling me about

9

the drugs, do you recognize those drugs and which  
ones do you recognize?

10

A. I recognize three of them.

11

Q. Which ones are those?

12

A. Quinidine, verapamil and

13

amiodarone.

14

Q. Okay. And do you recognize

15

them, sir, as drugs used in the treatment of heart  
disease?

16

A. With respect to quinidine, yes.

17

Q. Quinidine is used for heart

18

disease. What about verapamil and amiodarone?

19

A. I do not recall right now their

20

pharmacological reaction.

21

Q. My question then with respect

22

to those three drugs that you do recognize is this:

23

in 1981 when you were doing your analyses, were you  
aware of a cross-reactivity problem with digoxin in

24

25





1  
2 respect of any one of those three drugs? Just, were  
3 you aware of them?

4 A. I'm trying to answer your  
5 question. I was aware of some references in the  
6 literature. Well, with respect to quinidine -- I  
7 think perhaps I should go by one drug. With  
8 respect to quinidine I'm aware of references in  
9 the literature with respect to the possible elevation  
10 of some form of digoxin levels on a combined therapy  
11 with this drug. However, as I recall it, the  
12 mechanism is not cross-reactivity, at least, the  
suggested mechanism is not due to cross-reactivity.

13 Q. Whatever it's due to, do you  
14 recognize that it may produce apparently elevated  
15 digoxin levels when submitted to RIA testing?

16 A. There have been some reports  
17 that it may produce this but not due to a mechanism  
of cross-reactivity with the RIA antibody.

18 Q. All right, you are being precise  
19 and that's fair, but the effect of it for somebody  
20 reading the test would be to produce apparently  
21 elevated levels. Whatever the mechanism may be, the  
22 effect of it is that these levels are elevated.

23 A. To some extent, that's right,  
24 may be elevated is our literature articles.  
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Q. And I think you were careful, sir, to use the present tense in your answer to the effect that you are aware. My question was a bit more specific. Were you aware in 1981 of this phenomenon insofar as quinidine is concerned?

A. At some point in 1981 or 1982, I cannot exactly recall when I came across, you know, these studies in the literature.

Q. May we take it, sir, that quinidine is not something that you checked with respect to HPLC testing to see whether it came off. May we take that as a fact, it falls into the same category as furosemide?

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A. Well, you could use different techniques of analysis for quinidine, and I would use - as far as I know there is no RIA for analysis of quinidine.

Q. I am sorry, I will try and be more specific. As I understood it on HPLC testing you did account for spironolactone and you ran that off and you checked it, you didn't account for furosemide, and am I correct you didn't account for quinidine?

A. I did not specifically study quinidine for separation.

Q. On your HPLC?

A. Yes, as I recall it.

Q. All right, moving next to verapamil, sir, were you aware in 1981 of a cross-reactivity effect between verapamil and digoxin?

A. With respect to the other drugs really my recollection of the literature I would have to refresh my memory on it, I don't recall it right now, I am sure I have seen articles describing some.

Q. Let us just ask for the present then, sir, we are asking you today, sir, are you aware of a cross-reactivity effect under RIA testing between verapamil and amiodarone, are you able to tell us





E.2

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today are you aware of that, or are you not?

3

A. No, I am not. I should qualify,

4

I recall reading literature accounts suggesting

5

possibly that this may happen but it didn't leave a

6

strong enough impression on my mind to be concerned

7

about it at the present time.

8

Q. I take it it didn't leave a

strong enough impression on your mind back in 1981?

9

A. Whenever I read it.

10

Q. It wasn't a concern to you I

11

take it then in 1981 insofar as the tests that you

12

were doing?

13

A. Not early in 1981, no.

14

Q. Was it a concern to you at any

15

time in 1981 when you were doing these tests that it  
might be showing?

16

A. Again, we have tested some

17

drugs for cross-reactivity. I would have to go back,

18

you know, and look through our research notes to make

19

absolutely sure that these drugs were not included,

20

I don't recall at this time.

21

Q. You don't recall at this time?

22

A. No.

23

Q. But you can check your notes and

24

advise us.

25







E.3

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A. Pardon me?

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Q. You can check your notes.

4

A. Yes, I can certainly do that, yes.

5

Q. Moving to another area, sir.

6

Also in the realm of RIA reaction with other things.

7

There has been reference made to the recent research

8

in Vancouver which has identified what I will call a

9

something in the serum of infants which apparently

10

cross-reacts with digoxin antibodies, you are familiar

11

with that research and you gave evidence about it  
yesterday?

12

A. Yes, I am familiar with the

13

report that was produced.

14

Q. And as I understand it, at least

15

the article that I have seen was published in April

16

of 1983 in the New England Journal of Medicine, have

17

A. Yes.

18

Q. Is that the article that you

19

referred to?

20

A. That's right.

21

Q. And is that when you first became

22

aware of this particular something?

23

A. I think I first, before I was

24

able to obtain a copy of the article I believe I was

25





E.4

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aware of it by indirect contact, I may have heard it

3

described by media as I recall it before.

4

Q. Was that some time in early 1983?

5

A. This was some time before. Yes,  
some time in either March or early April, I forget now.

6

Q. Of this year?

7

A. Of this year.

8

Q. And that is when you first became

9

aware of this something might exist or someone had

10

identified this something?

11

A. That's right.

12

Q. Now I gather that the effect of

13

this something is that it may create the appearance  
of digoxin in serum when in fact digoxin is apparently  
not present?

*He means "actually"*

15

A. That is correct.

16

Q. And as I understand it, sir, in

17

1981 you yourself, or your Laboratory, did your own

18

study of digoxin in children who had not been

19

receiving digoxin, and you did not detect this

20

something, is that right?

21

A. That is correct, sir. Our tests

22

did not show this something, if I may refer to it, to

23

the same extent as was described in the report that  
you mentioned.

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E.5

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Q Well, let's be quite clear on this then. Did your tests show a something, and was it just a matter of the level of the something, or did they show nothing?

A Well, as I mentioned previously the highest current result that was produced by my team in this research was 0.5 nanograms per millilitre, the apparent digoxin.

Q Is that the highest for the Vancouver research or is that your highest?

A That is our highest.

Q So you did in your own research find a something, it is just that the level of the something was not as high as Vancouver, is that fair?

A Well, I'm not sure I found something, there was an apparent reading the highest of which was 0.5 nanograms per ml. As a result of that I have established a cutoff point which I described yesterday.

Q A which point?

A A cutoff point.

Q Well, what you are saying then is what you may have been detecting was simply an error in the method itself, or a factor in the method itself which gave a reading which does not really reflect a something?







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A. With some background: no specific difference with the RIA antibody which I regard as not specifically, which is present in all RIA procedures, not only digoxin but other drugs.

Q. So you regard it as something that may well be inherent in your procedure itself?

A. That's right.

Q. So in that sense at least you did not find a something that they apparently found in Vancouver, unless the something in Vancouver is a problem inherent in the method itself?

A. Well, my results, I'm not sure, my results did not confirm, our results did not confirm the results of the Vancouver group, that's right, from digoxin.

Q. Incidentally, these results that you have found, have they been published anywhere in the scientific literature?

A. They are being prepared for publication hopefully next year in Los Angeles.

Q. And these are the studies that you are going to look for and produce literature on among other things?

A. Yes, that was one of the results that I was asked to produce.





E.7

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Q. Now the last area insofar as interaction between the digoxin RIA procedure and other substance is concerned relates to something that you said yesterday in response to a question by Mr. Lamek. Mr. Lamek asked you whether you were aware of any endogenous substance manufactured by the body itself which cross-reacts with digoxin. Do you recall him asking you that question, I am just asking you if you recall?

A. I cannot recall the question. As I recall it Mr. Lamek asked me if there is digoxin produced in the body.

Q. Well, I have the question here and I don't need to read it to you for the purpose of suggesting your memory is faulty but I just have a question from yesterday's transcript at page 144 and I just want to read it to you and perhaps refresh your memory where Mr. Lamek said:

"Q. Now other than the known substances which you have told us about this morning, the metabolites of digoxin .."

THE COMMISSIONER: Just a minute, please, is there one for me? Page 144?

MR. STRATHY: About line 16.

THE COMMISSIONER: What about one for the witness?

(2)





E.8

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MR. LAMEK: Yes, I have one for him too.

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THE COMMISSIONER: Yes, all right.

4

MR. STRATHY: Q. I am not at all

5

trying to criticize Mr. Cimbura's recollection on this,

6

I can't remember what I had for breakfast one day to

7

another. You were asked that question at line 16, sir:

8

"Q. Now other than the known

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substances which you have told us

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about this morning, the metabolites of

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digoxin and the other two or three

12

drugs that you have mentioned, are you

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aware of any endogenous substance,

14

substance manufactured by the body

15

itself, that is cross-reactive with

the digoxin antibody?"

And your answer was:

16

"A. No, not on the basis of published

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information, literature, in humans, no."

18

Now, looking at the transcript I

19

assume you recall that question and that answer? It

20

confirms my notes, and do you recall giving that, sir?

21

A. Yes, I recall that.

22

Q. Thank you. I just note from

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your answer that you were careful to qualify it by

24

saying:

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E.9

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"No, not on the basis of published  
information, literature, in humans, no."

And I was going to ask you are you aware of literature  
dealing with an endogenous substance which is cross-  
reactive with the digoxin antibodies in animals, and I  
can be specific. Are you aware of this in rats and  
rabbits that suggest there may be an endogenous  
substance that cross-reacts with digoxin antibody in  
rats and rabbits, are you aware of any research in  
that regard?

A. Yes, I am aware of some research,  
I have a hazy recollection of this particular research,  
but as I recall it there was a reference - well, it  
was on animals, I believe it was rats, and the  
reference there was possible immuno reactive substance,  
but as I recall it not really antibody to RIA, this  
was another process that may have been enzyme-  
immunassay rather than radioimmunoassay. That is my  
recollection, I am a little bit hazy on this, it is a  
long time ago when I came across those articles.

Q. How long ago was it that you  
came across those articles?

A. Perhaps last year as I recall it,  
or before that.

Q. Just to be clear then, those





E.10

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articles did suggest there may be some endogenous

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substance in rats and it gave an apparent digoxin

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reading on a procedure for the detection of digoxin?

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A. Well, that procedure which I

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recall not to be radioimmunoassay, it may have been

enzymeimmunoassay.

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Q. That is your recollection?

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A. Yes, that's as I recollect it.

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Q. That is your recollection, is it?

A. That is as I recollect it, that is right.

Q. And when you gave your answer yesterday and restricted it to humans, is that what you had in mind when you gave that answer that there was research perhaps indicating that in animals and you were just trying to be careful in your answer? Is that why you qualified it by in human?

A. Yes. In humans I have not seen literature, any published literature to that effect, other than, of course, the study by the Vancouver group which we are discussing.

Q. Would I be correct in understanding, sir, that this research on rats that you have seen has only come out in the last couple of years? Would that be fair, or do you recall?

A. As I recall it, it may be, yes, a couple, the last couple or three years.

Q. Just a few more questions, sir, and I will be done.

In terms of what one tests using the RIA procedure, would you agree with me that the best way to test, if you are trying to find out pre-mortem







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levels is pre-mortem blood?

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A. May I qualify? For testing it doesn't really - your question implies with respect to interpretation.

5

6

7

Q. That is a good point. In terms of testing you can find the amount of X in just about any sample that is submitted to you?

8

9

A. Yes.

10

11

12

Q. But in terms of interpreting the results would you agree with me that in terms of accuracy of interpretation the most desirable thing to have is pre-mortem blood?

13

14

A. Yes. Pre-mortem blood, I should qualify, taken at a suitable time, you know, to the incident in question.

15

16

17

Q. Another good point, Mr. Cimbura. You would not want to take it too close to the time of the last digoxin administration?

18

19

20

A. Well, that, as well as you wouldn't want to have blood taken a week before whatever incident is being investigated.

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Q. Fair enough. And dealing with this question of the last dose of digoxin in terms of reliability of the reading, do you know from the literature, sir, or from your own experience, how long





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a waiting period should take place between the last administration of a digoxin and the testing itself to be sure of accurate results?

A. To be sure of accurate - to be sure of better interpretation rather than accurate.

Q. Fair enough.

A. The accuracy of the results has got nothing to do with the timing.

Q. I understand. I am sorry.

A. Well, as I have tried to describe yesterday, briefly, the --

Q. Well, I am just asking you if you can help us with the time, sir. We understand the mechanics, but the time.

A. Well, 4 to 6 hours after the dose.

Q. That is your evidence you should wait 4 to 6 hours?

A. Well, that would be because of the pharmacology of digoxin distribution.

Q. I understand that. I just want to be clear on your evidence, sir.

A. Yes.

Q. As to what you say is a desirable waiting period to be sure of proper interpretation.





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2

And are you saying 4 to 6 hours?

3

A. Well, that is if I had a choice.

4

Is that right, if I had a choice?

5

Q. Yes.

6

A. Well, I would, if I had a choice,  
blood taken, let's say, about 6 hours after would be  
acceptable to me.

8

Q. Would that be the best time from

9

your point of view?

10

A. About that.

11

Q. About 6 hours? All right.

12

Now I just finished asking you about  
pre-mortem blood, and I am going to ask you about  
post mortem blood in relation to digoxin levels pre-  
mortem. And would you agree with me that the next  
best source after pre-mortem blood would be post  
mortem blood for the interpretation of digoxin  
levels?

18

A. That is right.

19

THE COMMISSIONER: Well, it can't be.

20

It can only be two, can't there? You can't have more  
than a third kind, or is there?

21

MR. STRATHY: Tissues, for example.

22

THE COMMISSIONER: Oh, I see.

23

MR. STRATHY: As opposed to - I was

24

25







1  
2 talking in terms of other things that might be  
3 sampled.

4 THE COMMISSIONER: Blood is better  
5 than tissues?

6 MR. STRATHY: Q. Has the Commissioner  
7 expressed that accurately, Mr. Cimbura? Is blood  
8 better than tissue in terms of interpretation? In  
9 terms of desirability from your point of view?

10 A. In post mortem material, yes,  
11 blood would be my - post mortem blood would be in my  
12 view my specimen of choice.

13 Q. Now just to clarify one or two  
14 points. You were asked yesterday about your measure-  
15 ment of tissue, and you mentioned that when you are  
16 expressing your tissue results you do it in nanograms  
17 per gram, so you analyze a sample of tissue and you  
18 have a reading of 100 nanograms per gram. And you  
19 went on to say that the tissue itself is measured per  
20 grams of wet tissue.

21 A. Yes.

22 Q. Can you explain, please, what  
23 you mean by wet tissue?

24 A. The tissue is weighed in its  
25 wet form as opposed to drying it by an artificial  
process.





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Q. All right. So do I understand then when you use "wet" you simply mean the tissue as it comes or as it is presented to you from the original sample?

A. That is right.

Q. Whether that be the autopsy sample or the same that was stored in fixative or the sample from the exhumed body; is that right?

A. That is right. What I mean is in its wet form as opposed to let's say drying it in the oven and drying it, because there is some literature, results are given in terms of dry weight rather than wet tissue weight.

Q. All right. Let me just ask you something again. It is a question from a lay person, but would I not be correct in understanding that a tissue sample taken immediately post mortem would be, if you will, wetter than a tissue sample taken on exhumation? There is a drying out process after death.

A. It may be. That is one of the problems with exhumed tissue is that really there may be a process of drying and --

Q. In technical terms hydration takes place?





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A. Pardon me?

3

Q. I may be wrong.

4

A. Dehydration.

5

Q. Dehydration takes place. All

6

right. So that the exhumed tissue will have dried  
out over a period of time?

7

A. Generally to some degree, yes.

8

Q. One last point, sir. The

9

Commissioner asked you yesterday whether a gram may

10

be similar to a millilitre and you mentioned that the

11

weight could be close to the same, depending on the

12

substance that one was talking about, but I don't

13

understand you to mean that you can treat a nanogram

14

per millilitre reading in fluid or serum to be the

15

same as a nanogram per gram reading in tissue.

16

You can't say that if you find 10

17

nanograms per gram per millilitre in fluid that you

18

will also find 10 nanograms per gram in tissue of the  
same substance. You weren't trying to say that, were  
you?

19

20

A. I am not sure if I get your  
question.

21

22

Q. Well, I may have by trying to

23

clarify something may have confused you and the  
Commissioner.

24

25







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THE COMMISSIONER: Well, what I thought

3

I was trying to do was to find out whether a milli-

4

litre of substance was roughly equivalent to a gram of

5

substance and I thought the answer was yes it was, but

6

it would depend upon the substance and assume its

7

properties.

8

THE WITNESS: If I may qualify it

9

somewhat or illustrate it perhaps more: one millilitre

10

is approximately one-thirtieth of an ounce.

11

THE COMMISSIONER: All right.

12

THE WITNESS: One gram is approxi-

13

mately one-thirtieth of an ounce.

14

MR. STRATHY: Q. All right.

15

A. These are approximations.

16

Q. But my question was directed at

17

this, sir: if we see from a particular child a level

18

in the blood of, let us say, 5 nanograms per millilitre

19

of blood, we should not expect that the tissue from

20

that child taken at the same time and under the same

21

circumstances would also show 5 nanograms per gram of  
tissue?

22

A. Oh, of course not. The tissue

23

may be entirely different.

24

MR. STRATHY: Exactly. That is all

25

I wanted to make clear. Thank you.





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THE COMMISSIONER: Thank you, Mr.

3

Strathy.

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Mr. Marshall?

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MR. MARSHALL: I think I have no  
questions at this time.

6

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THE COMMISSIONER: All right. Thank  
you.

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Mr. Buhr?

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10

11

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MR. BUHR: I think in light of what  
has happened, sir, the few areas that I will be  
addressing to Mr. Cimbura, are better left for his  
return engagement.

13

THE COMMISSIONER: Miss Goodman.

14

CROSS-EXAMINATION BY MS. GOODMAN:

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Q. Mr. Cimbura, in your testimony  
in chief you mentioned a list of drugs other than  
digoxin which are chemically similar to digoxin. You  
mentioned them again this morning. You mentioned  
lanatoside C, deslanoside and digitoxin.

19

Is this an exhaustive list?

20

21

A. No. I believe there are some  
others described. I used these as examples.

22

23

Q. Are you able to name any other  
drugs which fall into this category?

24

25

A. Could I refer to some notes?





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THE COMMISSIONER: Oh, I think so, if

3

it would help.

4

MS. GOODMAN: Certainly.

5

THE COMMISSIONER: Are these digoxin-  
like drugs?

6

7

MS. GOODMAN: That is right. They are  
drugs which are chemically similar to digoxin.

8

9

10

11

THE WITNESS: Yes. If I may refer to  
the literature supplied by the manufacturers of the  
particular RIA package we are using, and in this  
literature they have a table.

12

13

THE COMMISSIONER: How many are there?  
How many drugs are there? Would there be a dozen or  
so?

14

15

THE WITNESS: About 11 drugs.

16

THE COMMISSIONER: Probably it would  
be easier - is it possible to file that document?

17

THE WITNESS: Pardon me?

18

19

THE COMMISSIONER: Can we file that  
document? Is that your only copy? If we make a copy  
of it --

20

21

THE WITNESS: Yes, that is my only  
copy.

22

23

24

THE COMMISSIONER: Well, I think the  
easiest thing, Miss Goodman, we will make it an  
exhibit.

25







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G/BB/ak

MS. GOODMAN: Certainly.

3

THE COMMISSIONER: Rather than

4

go through that, could we give that to

5

Miss Goodman, please, the document and, if it's

6

important, we might make it an exhibit.

7

MS. GOODMAN: I do think it's

8

important that the drugs be listed.

9

THE COMMISSIONER: Yes. What

10

number are we at?

11

Exhibit No. 4. What's the title of

12

it, Miss Goodman?

13

MS. GOODMAN: The title is RIA

Phase Digoxin Reagents System for --

14

THE COMMISSIONER: Well, let's

15

give it a short title, please.

16

MS. GOODMAN: Let's call it

17

"RIA Phase Digoxin", and it is Beckman. It is

18

headed Beckman, so it is obviously from the

19

Beckman Company.

THE COMMISSIONER: Yes, all right.

20

MS. GOODMAN: Q. Where precisely

21

is that list?

22

A. It is at one of the end

23

parts of the - perhaps on the other side.

24

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Q. It would be the list that begins with lanatoside C then and talks about specific performance characteristics and cross-reactivity?

A. That's correct.

Q. Thank you. Would you believe then that that would be the exhaustive list of the drugs which are chemically similar to digoxin?

A. Yes, I can think of no other ones, other than what we have discussed already.

Q. And was there any particular reason you mentioned the examples that you did or were they simply that, examples?

A. Well, there may have been one reason that, as I recall it, lanatoside C exhibits ~~a~~ relatively more cross-reactivity than the other drugs mentioned in the table and I do not recall now whether this lanatoside, what is the cross-reactivity, related cross-reactivity for this lanatoside.

MS. GOODMAN: Thank you, those are all the questions I have.

THE COMMISSIONER: Right, thank you. Would you put that in as an exhibit for us, please.

MS. GOODMAN: Certainly. A number of





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people are requesting it. I showed them the list,  
Mr. Commissioner, should I --

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---EXHIBIT NO. 4: Document entitled "RIA Phase  
Digoxin", Beckman Company.

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THE COMMISSIONER: And then I

think, Mr. Registrar, if you keep your eagle eye on  
it you might just put it down on that stand so that  
counsel may look at it but not steal it.

MR. LAMEK: Mr. Commissioner, may  
I suggest that we can have copies made at the break  
which I would think is coming along fairly shortly,  
rather than put it in a place of danger.

THE COMMISSIONER: Well, all right.  
Well then, we will just see because I'm going to,  
at the first lengthy, or at least anticipatory  
lengthy cross-examination we will take a break.  
Miss Kately - Miss Kately, is it?

MS. KATELY: Correct.

THE COMMISSIONER: Miss Kately, are  
you cross-examining?







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MS. KITELY: Yes.

3

THE COMMISSIONER: And how long do

4

you expect to be?

5

MS. KITELY: Ms. Symes estimated

6

between 20 and 30 minutes.

7

THE COMMISSIONER: How long do you

8

estimate because you are the acting?

9

MS. KITELY: Well, closer to 30

10

than 20, sir.

11

THE COMMISSIONER: All right. Well

12

now, would you like to start now or would you like  
to start after the break?

13

MS. KITELY: I would prefer to

14

start after the break, sir.

15

THE COMMISSIONER: All right. Well

16

then, that problem is solved and we will rise now  
for 15 minutes.

17

---Short recess.

18

---Upon resuming.

19

THE COMMISSIONER: Yes, Miss Kitley?

20

MR. YOUNG: Mr. Chairman, my

21

questions arise out of Miss Goodman's questions, so,  
I thought it would be appropriate to ask them now.

22

THE COMMISSIONER: Yes, all right.

23

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CROSS-EXAMINATION BY MR. YOUNG:

3

Q. Mr. Cimbura, this morning

4

Miss Goodman asked you some questions with respect

5

to chemically similar drugs with respect to digoxin.

6

Now, I understand Exhibit 4 is going around, copies

7

of it. I wonder if I might have a copy?

8

THE COMMISSIONER: Yes.

9

MR. YOUNG: Q. Again, I wonder

10

if you could direct me as to where I would find the  
list of 11 chemicals in the drugs.

11

Now, I just would like to go over

12

these drugs, and you will forgive my pronunciation

13

of them, but I'm curious to know whether or not you

14

are aware if any of these drugs are ~~endigenously~~  
produced. The first one would be lanatoside C.

15

A. Not as far as I'm aware, no.

16

Q. How about the second listed on

17

there. You have a copy, do you not? Do you have

18

a copy of the list I'm looking at?

19

A. Yes, I have.

20

Q. Great. The second is

21

digoxigenin.

22

A. That is digoxigenin.

23

Q. All right. Would that be

24

digoxin produced?

25





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THE COMMISSIONER: I'm sorry, what

3

is the word?

4

MR. YOUNG: I'm sorry, my under-

5

standing of an ~~and~~ogenously produced drug is one

6

that would be originating from within the body.

7

THE COMMISSIONER: Endogenous, isn't

8

it?

9

MR. YOUNG: Endogenous. That too

10

is my pronunciation.

11

THE COMMISSIONER: Well, that's

12

what you mean.

13

MR. YOUNG: That's what I mean.

14

THE COMMISSIONER: All right. And

15

the answer is for what?

16

MR. YOUNG: Q. The answer to the

17

first, in speaking of lanatoside C is no, is that

18

right, Mr. Cimbura?

19

A. That's right.

20

Q. And for the second?

21

A. For the second digoxigenin is

22

one of the metabolites of digoxin.

23

Q. I see, all right. Do you know

24

of any other source for that drug beyond the

25

metabolizing system that you have described to us

yesterday? Is that the only way that it would get







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into the body?

3

A. Well, that and of course if a  
pure chemical was administered.

4

5

Q. All right. The third one,  
and I'll ask you to pronounce them because I'm way  
off base. The third one on the list, I'm asking the  
same question.

6

7

8

A. As far as I'm aware it's not  
endogenous in the body.

9

10

Q. Okay. And the fourth one,  
lanatoside B.

11

12

A. As far as I'm aware, it's not.

13

Q. Is your answer the same for  
digitoxin, the fifth one listed?

14

15

A. Digitoxin is not endogenous in  
the body.

16

17

Q. Would lanatoside A be endogenous?

18

A. I cannot now recall exactly  
what it is but I don't believe it is endogenous in  
the body.

19

20

Q. Okay, we're onto the second  
row there. Could you help me with the first one  
listed in the second row?

21

22

A. Pardon Me?

23

Q. Same question.

24

25





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A. Digitoxigenin, not endogenous -

3

well, it may be a metabolite of digitoxin.

4

Q. How about the next listed drug?

5

A. Ouabain, not as far as I'm

6

aware of.

7

Q. Let's just work our way down

8

the list. The next one, testosterone.

9

A. I'm not really certain the

10

next two. I should know that with regard to the

11

last three the cross-reactivity is very low, it is

12

almost negligible.

13

Q. Fine. Just for the assistance

14

of other counsel, I wonder if you would - well, I

15

would be happy to spell the last three listed drugs.

16

Perhaps the easiest way. The third from the last is  
t-e-s-t-o-s-t-e-r-o-n-e.

17

A. That's testosterone, that's

18

right.

19

Q. The next one is

20

p-r-o-g-e-s-t-e-r-o-n-e.

21

A. Progesterone, that's right.

22

Q. And the last one is

23

s-p-i-r-o-n-o-l-a-c-t-o-n-e.

24

A. Spironolactone. Spironolactone

25

is not endogenous in the body and, as I noted, the





1  
2 last three are extremely low cross-reactivity.

3 Q. Would it be correct, and I  
4 think I am simply stating the obvious here but,  
5 Mr. Cimbura, would it be correct for me to say that  
6 if an infant had never been administered the drugs  
7 that you have identified as not being endogenous,  
8 would it be correct to say that these drugs would  
9 have no effect on any RIA or other tests that you  
10 were conducting with respect to digoxin?

11 A. Would you repeat that question  
12 again, sir?

13 Q. I'm curious to know if the  
14 drugs that you have mentioned that are not endogenous  
15 would have any effect on any RIA tests for digoxin?

16 THE COMMISSIONER: If they hadn't  
17 been administered.

18 MR. YOUNG: Thank you.

19 Q. If they had not been administered.

20 A. If they had not been administered.

21 THE COMMISSIONER: If they had any  
22 and you couldn't produce it from the body. I think  
23 the answer to that is no.

24 MR. YOUNG: That's what I would have  
25 thought.

THE WITNESS: It's no, that's right.







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THE COMMISSIONER: I'm leading the  
witness something awful.

4

MR. YOUNG: I understand but I  
simply wanted to make that clear.

5

6

Those are all my questions.

7

THE COMMISSIONER: Yes, thank you.

8

Miss Kitely?

8

9

MS. KITELY: I have stolen  
Mr. Lamek's place, I hope I'm not hoarding his  
corner here.

10

11

CROSS-EXAMINATION BY MS. KITELY:

12

Q. Mr. Cimbura, can you tell me  
when you are testing for RIA what quantity of  
blood sample you require?

13

14

A. Well, our procedure is designed  
to use 0.5 millilitre of blood, whole blood.

15

16

Q. And when you are doing the  
RIA and the HPLC, how much do you use, of blood?

17

18

A. We can do that in two different  
ways. So that we can do the HPLC in two different  
ways. We can either, depending on what we want to  
do, we can either use, if there is some remaining  
extract after the RIA procedure, we can analyze that  
or else we can begin with an extraction of a fresh  
portion of the blood. The amount for HPLC would

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depend on the concentration of the drug in the  
blood.

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Q. Well, let's assume you are  
starting fresh and you are going to do RIA and HPLC,  
how much do you need?

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A. It would depend on the  
concentration. The HPLC technique, as we have it  
designed, is suitable for higher concentrations of  
digoxin in blood, at least that's what we were  
concerned with. Originally when we designed it the  
concentration that we would have to have at the  
beginning in the blood would be around 12.5 or so  
nanograms per millilitre and we have tried to reduce  
the sensitivity now to about 6 nanograms per  
millilitre. If the blood had that concentration,  
then we would need .5 millilitres of blood.

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Q. I'm sorry, .5 or .05?

A. Pardon me?

Q. .5 or .05.

A. .5 millilitres of blood.

Q. When you are testing tissue,  
what quantity of tissue do you require?

A. Normally we use .2 of a gram of  
tissue.

Q. Is that for RIA?





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A. That is for RIA, that's right,  
yes.

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Q. All right. And is it fair  
to say that most of the testing that you did was  
with respect to either blood or tissue and very  
little with respect to serum and plasma?

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A. Relatively less for serum and  
plasma, that's right, yes.

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Q. Is it possible for you to  
estimate it, and I appreciate this is very general  
terms, would you have tested as much as 70 per cent  
tissue and 10 per cent plasma and serum and 20 per  
cent blood? Can you give any kinds of ranges like  
that?

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A. I don't know exactly before I  
could give that to what testing are you referring to,  
testing in connection with the samples received  
from the police with regard to this investigation?

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Q. Yes.

A. Or just any samples at all.

Q. No, no, I meant with this

investigation, Mr. Cimbura.

22

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A. Pardon me?

Q. With this investigation, the  
samples that you received from the police.







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A. The majority were other than  
serum or plasma.

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Q. And of the majority, were  
they mostly tissue and not blood?

5

6

A. Yes, I would think so.

7

Q. And of the tissue that you  
received, was any of it frozen, did it come that  
way?

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9

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A. There was such a variety of  
tissues, and I haven't really gone over the entire  
report for the purpose of my appearance at this  
time. Some were received refrigerated, some were  
received, when I received them may not have been  
refrigerated. I would have to go specifically  
through all of them, you know, to give you an exact  
answer to your question.

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Q. Well, let's deal with what you  
do with them when they come to you. For example,  
with the blood. Do you put any preservative in it  
to keep it for future reference?

20

A. Do we put a preservative in it?

21

Q. Yes, do you mix it with any  
kind of preservative?

22

23

A. With respect to digoxin analyses?

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Q. Yes.

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A. Well, I'll have to qualify the answer to that. We provide containers for collection of blood which has a mixture of a preservative and an anticoagulant in it. The main purpose of this is with respect to other - preservative with respect to other drugs such as alcohol.

Now, in some of these specimens that were received in this investigation, the container may have been used by the pathologist who put blood into it. Again, I would have to refresh my memory on that.

Q. Well, I'm just looking generally.

A. Once I get the blood, I don't add any preservative to it.

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Q. Generally speaking the containers in which the blood comes have been mixed with an anticoagulant.

A. Would you say it again, please?

Q. Generally speaking, blood samples that come to you are in a container in which they have been mixed with an anticoagulant?

A. Generally from the point of view of all our investigations, not only this particular one.

Q. I appreciate that, but I am only asking you about this one.

A. This particular one I know that there were at least one that came in in container. I would have to refresh my memory on it and see whether there may have been more.

Q. And if they didn't come in in your container they would have come in the Hospital's containers which may or may not have had anticoagulant?

A. They would come in some other containers.

Q. But if they weren't yours you wouldn't know necessarily what was in the container?

A. Not unless I was told that, or it was reported to me.







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Q And was it usually reported to you?

A Perhaps not usually, sometimes.

Q And if it was reported to you would it be recorded somewhere on the intake charts for example?

A It may be recorded, yes.

Q Let's deal with the tissue. When it comes to you, in what form is it, has it been put with something, some preservative?

A Are we talking about the investigation of the babies, the death of babies?

Q Generally speaking the investigation of the death of babies, and is there a general rule about the way the tissue came to you. If there isn't please say so and we will deal with each individual when the proper time comes.

A Well, some tissues came - I would have to refresh my memory on that when I go through the individual tissues.

Q So we will deal with that --

A I think so, yes.

Q Now I understand that the investigation started at the end of March and that is when the samples started coming to you, am I correct?





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A. Some time in March, I don't have the date with me right now, March, 1981.

Q. Let us assume the end of March, 1981, shall we?

A. Yes.

Q. Now at that time you were only doing the RIA tests?

A. Well, at that time we started to develop and evaluate our RIA procedure, the RIA procedure that we could use later on.

Q. Well, let's put it this way, at some point in time you developed the HPLC to the level that you thought you could start using it, is that correct?

A. Yes, some time later, that's right.

Q. I understood you to say yesterday that that "some time" was in September?

A. That is, as I recall it, it may have been September, I didn't have yet a chance to - I didn't go over it.

Q. Does that mean that between March when the samples started coming in until September when the HPLC was perfected that you were only using the RIA tests?

A. At the beginning we were using





H.4

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only the RIA test, that is right, for some time, the exact periods of time I will have to go over each note and find out.

4

5

6

Q. Well, when we get to the individuals will the records that you produce show when you did the RIA test?

7

8

A. Yes.

9

Q. And will it show when you did the HPLC test?

10

11

A. There should be a record to that effect, yes.

12

13

14

Q. Now, can I ask you to assume for the moment that between March and September you concentrated on the RIA tests, is that an assumption you can make with me now?

15

16

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A. Between March we concentrated on the - as I recall it we concentrated on the development of the RIA tests first. After March for some period of time and then at some stage we also started to develop and evaluate the HPLC.

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Q. Is it fair to say when these samples initially came in at the end of March that you didn't have a technique?

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A. Didn't have the methodology.

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Q. You didn't have any technique to test?

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H.5

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A. In the procedure, we had equipment, an evaluated procedure that I would be satisfied with, that's right.

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Q. In fact that is why you suggested to the police that they go elsewhere with the samples?

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A. That's right.

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Q. And then they came back to you a few days later and you were then in a position where you had to develop a procedure and technique?

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A. That's right.

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Q. And would that have taken you a few weeks to develop?

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A. Well, it has taken more than a few weeks. As I recall it it was taking several months, but if you want specific dates, you know, I don't recall them right now.

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Q. You initially though were working on the RIA tests and I understood from your evidence yesterday that the HPLC was the second stage, is that not true?

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A. Well, we started to develop and evaluate the RIA procedure, that's right. The research on the HPLC procedure was started as I recall at some time later on.

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Q. I guess what I am getting at,





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Mr. Cimbura is, am I correct that at the beginning that you did the RIA test and at some later point you re-did RIA and HPLC test?

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A. With respect to what, the analyses of what?

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Q. Take samples from Baby X, let's say it came in in April 1981 and let's say you did an RIA on that in April of 1981, and let's say you developed the HPLC until it was at a stage that you felt comfortable with in September. Did you take that tissue from Baby X that was still around and re-do it using the HPLC and the RIA?

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A. As I recall it we started to apply the HPLC at a later stage than we applied the RIA to the specimens on the investigations. so there may be an interval of time, yes.

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Q. What I am getting at is did you take the sample that you worked on once and work on it again to come up with a confirmatory finding using the HPLC test?

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A. Either work on the samples or else use extracts that have been kept from previous work.

Q. Yesterday you indicated that the RIA wasn't too reliable because it didn't discriminate







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between metabolites and digoxin substances and you thought the HPLC was much more reliable, is that a correct statement?

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A. Well, I don't believe I used the words that RIA was not reliable, I don't recall it, that is the disadvantage of the RIA technique.

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Q. But the HPLC is much more reliable?

A. The HPLC gives me an added certainty, or added probability, I would correct myself what I am detecting is digoxin.

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Q. Generally speaking for all of the samples that you initially did only RIA on, did you at some later point, and I don't care whether it was September or whenever, but at some later point did you re-do those using HPLC?

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A. We may have, I would have to - with some samples yes, probably.

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Q. But it wasn't the general rule?

A. Well, we didn't have the HPLC technique, it was not developed until some time later on.

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THE COMMISSIONER: I am sorry, just so you understand. The problem is if you did an RIA test in April, when you completed your development of





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the HPLC test then did you re-do the test so that  
it would have the benefit of the HPLC?

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THE WITNESS: Oh, okay. As far as I  
recall it, both whenever it was possible.

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6

THE COMMISSIONER: It wasn't possible  
from March until September. So, let us assume then  
in September you mastered this HPLC test, then did  
you retest those that you had done between March and  
September with the HPLC test?

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THE WITNESS: With HPLC, yes, because --

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THE COMMISSIONER: You did, or you  
didn't?

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THE WITNESS: Whenever it was possible  
and there were so many specimens.

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THE COMMISSIONER: Okay.

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MS. KITELY: Q. Is it fair to say that  
whenever it was possible depended on whether you still  
had samples left over?

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A. That would be one factor.

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Q. What were the other factors  
about whether you would re-do it?

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A. Well, another one would be if  
there were findings, for example, that were negative  
by RIA.

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Q. You wouldn't bother?

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H.9

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A. No, I wouldn't bother to do HPLC.

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Q. And what other reason might

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there have been for not doing an HPLC?

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A. That is the only two I can think  
of right now.

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Q. Now, dealing with the tissue.

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A. Perhaps, I am sorry if I am not

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very clear, but the investigation involved specimens

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of multiple numbers from, as I recall it, 24 different

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babies, there were a lot of different specimens and

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I would like to apologize if I cannot recall exactly

12

what was done on each specimen.

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Q. Well, Mr. Lamek would be speaking

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if I was asking you about individuals, I am really

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just getting at general rules if there were any?

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A. Generally speaking, when there

17

was a sample available, or an extract available and

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the levels obtained by RIA were positive and in the

19

range that we could detect by HPLC then we would do

HPLC analysis.

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Q. Now, is it fair to say as a

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general rule that when you did do HPLC analysis later

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on you did it on tissue and not blood?

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A. Oh no, as far as I recall we did

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HPLC on blood as well.

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H.10

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Q. And of course your records will be produced for each sample which would show what you have for HPLC?

A. Yes, and also my results are worded to distinguish whether only HPLC was used, or whether both were used, or whether just RIA was used, my results are worded in such a way to distinguish.

Q. I would like to stick with the tissue for a moment. Am I correct that the tissue was stored in something called a Klotz solution?

A. In some cases.

Q. And what is the difference in Klotz and other, who determined which solution the tissue would be stored in?

A. I don't know who would determine it, you are asking me to determine what the tissue should be placed into the Klotz?

Q. Yes.

A. I would think that is somebody at the Hospital for Sick Children.

Q. But you said sometimes Klotz, is there another solution that would also have been used?

A. I am sorry, I don't understand it.

Q. Well, are there a variety of different preservatives of which Klotz is one?





H.11

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A. There are some tissue, also mixed or contained in, as I recall it, in a medium called Eli medium and some tissues where of course there was a presence of embalming fluid, is that the question you are after?

Q. As a general rule, if there was one, was tissue preserved in Klotz more than any other kind of solution?

A. I would have to count the exact specimens.

Q. And the records that you are going to produce when we deal with the individual samples, will it indicate whether the tissue was in Klotz or something else?

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A. Yes. They will, and my report I believe also includes these factors.

Q. Now when you came to do the HPLC test, you had to deal with the fact that this tissue had been sitting in the solution for some period of months.

A. Yes.

Q. Is that right?

A. Well --

Q. You had to take the Klotz factor into consideration?

A. In consideration for what?

Q. Well, let me rephrase it. Did you when you did the HPLC on tissue take into consideration the fact that the tissue had been in a solution, be it Klotz or otherwise, and that that may affect the results of your test?

A. Whenever I have known the information that the tissue was contained in a chemical, it was taken into consideration for whatever reason, but I am not sure that I can answer the question as you worded it.

Q. Was the presence of the solution part of an equation that you dealt with when you were interpreting the HPLC tissue results?







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In other words, did you look at the numbers of the results achieved on an HPLC and say to yourself we have to do something about the presence of solution, Klotz or otherwise, and how are we going to eliminate that as a factor? Did you go through that process?

A. Well, I was concerned with the effect of the Klotz solution on the stability of digoxin.

I was concerned with the effect of Klotz solution on the diffusion of digoxin from the tissue into the surrounding medium and other factors.

Q. Well, in fact a Klotz can have a significant effect on a reading, can it not, in the sense that over a period of time that the tissue has been in a solution it can be very substantially diffused, to use your word?

A. Over a period of time the drug --

Q. The drug --

A. -- can, in my view, can diffuse from the tissue into the surrounding medium.

Q. So then you have to measure not only the tissue but also the surrounding medium?

A. That is right.

Q. And you went through that analysis





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in each case?

A. We measured, as I recall it, the surrounding medium in most cases by RIA only, and was suitably reported as such.

Q. And that will show up on the records when we see them?

A. Yes. That will show on the records, yes.

Q. If I could deal for a moment with the actual process, the HPLC, I had some difficulty understanding a couple of things yesterday. I understood you to say that it involves a process whereby a sample is driven through a column containing special absorbent material; is that correct?

A. Essentially, yes.

Q. Now the importance of it is that the speed with which something emerges at the other end identifies what it is?

A. Is characteristic to a given compound.

Q. Now when you were recording the HPLC, do you have some sort of a graph or do you - do you keep a graph on, say, sample X to show that metabolite 1 came out at a certain time and metabolite 2 at another and digoxin at another?





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A. Well, the times for the metabolites, this was part of our research effort, and I have a record of the times, yes.

Q. And that is all on the records of the individual samples?

A. For individual metabolites.

Q. Yes?

A. Not for - I am not sure, are you asking me whether we tested for metabolites specifically in each sample? Is that what you are asking me?

Q. Well, I understood you to say that on the HPLC the metabolites come out at a certain time and digoxin comes out at a certain time.

A. Yes.

Q. My question to you is do your records show when each of those came out or will they only show when digoxin came out?

A. When we analyzed the actual samples the only time fraction we were collecting from the HPLC column in the majority of cases was the fraction corresponding to the time of digoxin.

Q. Can you give me an idea how long it takes for all of these substances to emerge from the column? Are we talking about a day or two minutes?







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A. Well, some emerge in a minute.

Q. I don't know whether I was clear -

Mr. Cimbura, what I was talking about, if you put a drug in --

A. Yes.

Q. -- at minute 1, when is the process finished?

A. It is a matter of - with some drugs it is a matter of minutes. With other drugs even when we studied the collection for as long as 40 minutes or even longer, and I cannot recall now, they still did not move from the column, so that we didn't wait for days. You know, it could have been days, but we didn't wait that long.

The only information that I record is that they do not elude from the column within, let's say, 40 minutes.

Q. And would that be recorded on the documents you are going to produce?

A. Well, no, that is not on my report. This was part of our research, evaluation of the HPLC.

Q. Well, given that digoxin - and I just want to make sure I understand this - to do a standard test using the HPLC (standard, let's say





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1  
2 average), if you put it in at minute 1, do you expect  
3 it to be finished by minute 5 or 10? I don't care.  
4 I just want to have a frame of reference, Mr. Cimbura.

5 A. Well, the digoxin, depending on  
6 the conditions. These times, of course, vary with  
7 the conditions that you use, the column --

8 Q. Well --

9 A. -- the composition of the  
10 elements and so on, but just a general time frame,  
11 digoxin may come out in 10 to 12 minutes. Something  
12 like that.

13 Q. Thank you. That is what I was  
14 looking for.

15 A. Yes.

16 Q. To say 10 to 12 minutes you are  
17 expecting the column to have cleared; all of the drug  
18 to have come through?

19 A. Not all of them. Digoxin. Some  
20 may come before that and some may come later.

21 Q. That was my next question. Does  
22 digoxin come before or after the metabolites?

23 A. When the analysis is done in  
24 the reverse phase some of the metabolites come before  
25 digoxin and one, as I recall it, did not elude until  
at least 40 minutes, so it would be after. But, you





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know, this is my recollection from my research notes.

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But some metabolites do come before digoxin.

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Q. Right. Let's just use our same 12 minutes. Is it fair to say that a metabolite might come out at minute 2 and another one at minute 9 and digoxin might come out at minute 7, or a combination of those?

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A. Well, let's say if digoxin comes at minute 12 then some of the metabolites may come before that, and I do not recall exactly at what stage they come out, but it would be before the time of digoxin.

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Q. You used the term reverse phase, and you used it yesterday in conjunction with normal phase. Would you define the two of those please?

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A. They essentially deal with the use of different columns and different elements in the chromatography. For example, for the reverse phase, HPLC, the column is coated, column V was a Microbondapack C18, which is a type of silica absorbent coated with C18 carbon, hydro-carbon. In a normal phase the column is - does not have that coating, and as a result of that there is a change in polarity.

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Q. So the phases are with reference







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to the substance of the absorbent material that is in  
the column?

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A. That and the composition of the  
element or the mobile phase.

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Q. Now to go back to my minutes 1,  
7 and 9, I want to simplify this: am I correct that  
Beckman's, the people from whom you got the kit, said  
that the standard would be, for example, metabolite  
1 would come out at minute 2, metabolite 2 will come  
out at minute 9, and digoxin will come out at minute  
7?

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Is that the kind of thing that Beckmans  
told you?

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A. No. Beckman - I believe Beckman  
referred to only RIA and not to HPLC.

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Q. Right. I understood you to say  
that there were standards that you applied using the  
HPLC initially, and that later you substituted your  
own standards. Am I accurate in that?

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A. I don't recall that I said that.  
If you wish me I will clarify that.

Q. Well, let's do it a different  
way. In looking at the results --

A. It is not essentially true, no.

Q. Okay. I will accept that for





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now.

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Now in looking at the results of the  
HPLC, did you have a standard to say --

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A. Yes.

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Q. -- that minute 2 was a

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metabolite?

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A. Pardon me? Yes, we had

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standards.

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Q. Where did you get the standard?

10

A. The standards were obtained or

11

purchased from various pharmaceutical houses as  
reference standards.

12

Q. All right. And to be extremely  
simple would a pharmaceutical house X say 2 minutes,  
6 minutes, 9 minutes? Is that the kind of thing that  
the standard would show?

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A. No, but --

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Q. I realize I am being simple but

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I need to know what a standard is.

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A. A standard is a reference

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standard or the drug in its as much as possible pure  
form and it is available quite usually as a powder.

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Now when I received the standard, some  
of the metabolite standards, for example, I had to  
request from Europe and it was quite difficult to get

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them. But the behaviour of these standards on the HPLC, this is something that I did not receive from the manufacturers.

Q. Sorry. You did not receive them?

A. No. The information as to the times, as you mentioned, 7, 8, 9.

Q. Right.

A. I did not receive from the manufacturers.

Q. So you got some from Europe, and did I understand you to say that you used different standards for HPLC later on?

A. No. What I said is that with the RIA procedure that we purchased from Beckman, the kit. This kit comes supplied with standards for the RIA procedure.

Initially in our evaluation of the RIA procedure we have used those standards, and then later on we have changed to preparing our own standards obtained from other companies.

Q. Obtained from another company?

A. Where the pure standard was obtained from other company.

Q. And will the records that you







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produce show whether you used the Beckman standard  
or another standard for the purpose of interpreting  
the RIA results?

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A. It may show it, exactly when we  
started to use our own standards. From there on we  
would always be using our own standards.

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Q. Why did you change on the RIA?

A. Well, one other reason was and  
I believe I touched on yesterday, was that since the  
majority of our work dealt with specimens other than  
blood, and even in blood the way we used the RIA  
procedure with the preliminary extraction process one  
is left with the extract at the end, which is made up  
in saline solution, and we wanted to prepare our  
standards in the same medium.

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BMB.jc

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Another reason was just that general reason that, as we do with all testing for all other drugs, we prefer to prepare our own standards for the analyses. This is common to all our other procedures.

Q. You used a phrase yesterday which is probably the longest one that I have ever heard, and I'm going to say it and you can correct me if my pronunciation is wrong: gas chromatography mass spectrometry?

A. Yes.

Q. That's all one phrase, is it not, referring to one procedure?

A. Yes, it is the use of two instruments joined together, that's right.

Q. Right. Now, did I understand you to say that you used this procedure for one confirmatory test in one baby's sample?

A. We have used that in one case, that's right, yes.

Q. But I understood from your evidence yesterday that that is a procedure that you use in drugs normally when you're not looking for digoxin. It's a standard test?

A. I wouldn't call it a standard test, it's a test that we use quite usually, yes,





J.2

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that's right, for other drugs than digoxin.

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Q For other drugs. In fact, it's not really useful for digoxin because of the molecular weight of digoxin.

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A Because of the molecular weight, the water solubility of the - sorry, the chemical nature of digoxin. Those are developed factors why it makes it difficult to apply it for the analyses of digoxin in body specimens considering the very low concentrations of digoxin that we have to see and detect.

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Q Well, I understood your evidence from yesterday to indicate that that is a procedure that you deliberately didn't use at the outset when you were doing the digoxin testing?

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A At the outset?

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Q When you first started. You recognized that it was an inappropriate test for the reasons you have just indicated?

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A Yes, at the outset we did not begin with that procedure because it was my belief that from reading the various literature on the subject that the RIA and the HPLC would be more appropriate for the analyses.

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Q Well then, why is it you feel





J.3

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that having used this procedure later on that it is  
useful and it confirms anything?

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A. Because the identification of a  
drug by this particular procedure, I'm referring to  
gas chromatography and mass spectrometry provides a  
high probability of identification, perhaps more so  
than any other single procedure.

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Q. For drugs other than digoxin  
though?

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A. Pardon me?

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Q. For drugs other than digoxin?

A. It can be more readily applied  
to drugs other than digoxin.

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Q. But if you recognized that it was  
an inappropriate test to start out with, why are you  
suggesting that by using it once later on that it  
confirms?

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A. Well, because in that instance  
the result, you are able to obtain a positive result  
and, as I have mentioned before, positive result by  
mass spectrometry - by this combination of instru-  
mentation carries with it a high probability of  
identification of a drug.

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Q. But the results of that test  
standing alone are really not helpful?

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J.4

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A. The results of which test?

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Q. Of the gas chromatography mass spectrometry. The test that you did on the one sample using that procedure?

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A. I'm not sure if it was on one sample, it was in one case.

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Q. All right, one case. The results of that test, standing all by themselves without any RIA are really not very useful?

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A. Oh, they would be useful.

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Q. But you've indicated that it wasn't an appropriate test because of the molecular weight, so, how can the test itself be useful?

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A. The problems of the molecular weight and other chemical problems deal with the practicability or the ease of application of the technique to detect very low concentrations of digoxin in the body samples. If you do the test and if you have managed to overcome the difficulties and get a positive result, the result is very useful for the identification of the drug.

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Q. And the records that you are going to show about the test, it will indicate the one on which you did, where you used this particular procedure?

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J.5

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A. My report may not show that particular - may not show that because I have used that test, I have taken the positive result in my consideration before reaching a conclusion on the report of the particular case.

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Q. But that might not have been recorded, is that what you're saying?

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A. On my report. We have documents on it but in my official report there is no particular reference to it.

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Q. I want to deal with one last thing. With reference to the British Columbia test, did I understand you to say that the results might have had something to do with the mother having had digoxin?

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A. Yes, I believe I mentioned it in some context as a possibility.

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Q. So, does that mean if a mother who received digoxin during pregnancy or after pregnancy but while breastfeeding, then a child will have what would appear to be endogenous levels of digoxin even though the child has had no digoxin?

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A. Well, I wouldn't call it in this case endogenous, I wouldn't use that term, but it is a possibility that the digoxin from the mother's





J.6

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circulation may make it into the baby's circulation  
to some extent.

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Q. And that could be a factor  
affecting the results?

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A. Well, there would be digoxin,  
which would of course affect the results.

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Q. And in any of the analyses ---

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A. If this was true. I'm not  
sure whether it may have been, but it is a possibility  
that I raise.

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Q. Yes. In any of the analyses  
that you did during this investigatory period, did  
you ever receive information about whether the  
mothers of the children had received digoxin?

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A. In what kind of an investigation?

16

Q. In the investigation that we're  
talking about?

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A. The samples as received by the  
police?

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Q. Yes. Was there any effort to  
ascertain whether the mothers had received digoxin?

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A. I don't believe I have information  
whether they did or not.

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Q. But you have indicated that if  
they had, that that might affect the reading which you  
subsequently get?

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J.7

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A. To a small degree.

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Q. Yes.

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A. The Vancouver study, the results are, you know, relatively small.

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MS. KITLEY: Yes. Those are all my questions, thank you.

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THE COMMISSIONER: Thank you. Now, is anyone here for the Doctors? Miss Chown?

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MS. CHOWN: Mr. Ortved asked his questions yesterday.

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THE COMMISSIONER: Oh, yes, yes of course, that's right. All right, Mr. Olah.

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CROSS-EXAMINATION BY MR. OLAH:

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Q. Just one point that I wanted to clear up, Mr. Cimbura, that puzzles me. This separation technique or HPLC technique that you talked about, what it does is basically gives you a fingerprint of each metabolite that comes out, doesn't it?

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A. Well, I'm not sure whether I would call it a fingerprint. If you are testing for them, it gives you a result, whether the metabolites may be there and at what time they elude from the column, you know, if you intend to test for that.

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Q. Well, for us laypeople, would it be appropriate to describe the result is that for each





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metabolite you've got a different sort of fingerprint  
that characterizes what that substance is?

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A. It's characteristic, each  
retention time, or the time of elution of the  
metabolite from the column is a characteristic of a  
compound, but by itself is, you know, I think finger-  
prints are much more characteristic.

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Q. All right, it is an identification  
process in other words. Each metabolite has its own ---

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A. It's a separation process.

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Q. But the end result is that you  
get an individual sort of name tag or identification  
process for the metabolite. Isn't that what it is  
all about, reduced to its simplest?

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A. Would you repeat that again, I'm  
not sure I got that.

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Q. Well, what you get as a result  
of this test is an identification of each metabolite,  
a unique characterization?

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A. As a result of the HPLC test?

Q. Yes.

A. Characterization of ---

Q. Of a metabolite?

A. A metabolite, yes.

Q. Right.





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A. You get an indication of a  
presence of metabolite.

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Q. And each one is unique?

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A. The ones that I have studied  
are unique.

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Q. All right. And it is in that  
sense that I suggest that it's like a fingerprint in  
that you can look at the result and each one is unique  
to that particular substance?

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A. If I may go back. Perhaps the  
word "unique" is not correct, maybe I should refrain  
from it. The times from which the metabolite comes  
from the HPLC column is characteristic of ---

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Q. Of that particular drug?

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A. --- of that particular drug.

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Q. All right. Now, it is important  
to know what the individual time or characteristic is  
in order to be able to identify that drug, correct?

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A. Yes.

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Q. Because without knowing that  
fingerprint or name tag, you can't say what it is,  
correct?

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A. That's right.

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Q. Now, the Vancouver study that  
has been talked about seems to suggest that there





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might be the endogenous production of the digoxinlike substance in these infants that were studied, correct?

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A. They suggest there is an immuno-reactive digoxinlike substance.

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Q. Digoxinlike substance. Now, you don't have, or when you carried out your test you didn't have that information available to you, did you? That's a fairly recent study?

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A. When we developed our test?

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Q. Yes.

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A. Yes. No, that's right.

12

Q. And presumably this substance that was found in the Vancouver study would have its own identity or character in the HPCL test, would it not?

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A. It may.

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Q. And not knowing that there was a unique character when you were running your test, it may be that what appears to be digoxin on the test you ran may in fact be this digoxinlike substance that was found in Vancouver?

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A. Well, there is a possibility, but I think it is unlikely.

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Q. All right. And of course you're aware that the Vancouver study has also been

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reproduced to some degree, although, the end product  
is different in a recent Washington study. Are you  
aware of that?

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A. A recent Washington study?

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Q. Yes.

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A. I don't believe I'm aware of  
that, no.

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Q. Okay.

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A. Perhaps you could expand on that

for me.

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Q. That's the information that I was  
conveyed.

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MR. OLAH: Thank you, those are all  
the questions I have, Mr. Commissioner.

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THE COMMISSIONER: Thank you. Now,  
gentlemen, I will take you in whatever order you want.  
Usually I would call Mr. Manning first but there is  
no reason we can't have some other arrangements if  
you want to. Mr. Shanahan?

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MR. SHANAHAN: I won't be that long,  
Mr. Commissioner, so I'll go first.

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CROSS-EXAMINATION BY MR. SHANAHAN:

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Q. Mr. Cimbura, in your questions

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here and in the line of questions that's been put to  
you about digoxin, but just some that's come to my

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mind here, whoever directed you to do this testing  
for digoxin? I mean, obviously you were testing  
samples, I take it at first looking for toxic  
materials, any of which that could be present in a  
hospital that might be in overdose proportions in  
these tissues.





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Did you test for a wider range of drugs and then digoxin starts to appear, or did someone centre you right in on digoxin at the outset?

A. The function of the Toxicology Section of the Centre of Forensic Sciences test a wide variety of drugs, alcohol and chemical poisons by specimen. The reason we became specifically involved in the digoxin method development and analysis was because of the serious investigation of the babies at the Hospital for Sick Children.

THE COMMISSIONER: Mr. Cimbura, the question is were you asked at that time to investigate blood or the tissue for digoxin, or were you asked just to investigate the blood, or the tissue, or whatever you could find?

THE WITNESS: I am trying to recall. Digoxin was specifically mentioned by the investigators.

MR. SHANAHAN: Q. Who was it mentioned by, who directed you to test samples for digoxin as opposed to anything else?

A. Well, some of the investigators were Sergeant Warren, Sergeant Press, I'm not exactly sure which one.

Q. In any event, investigators







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I take it would come to you, would they come with  
samples in tow and give you these samples and say  
to test for digoxin?

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A. Yes. The investigators  
bring the samples and they request the analysis.

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Q. It perhaps wasn't your function,  
but obviously you knew this involved children at  
the Sick Children's Hospital, and you knew that  
there could be potentially many toxic drugs within  
the hospital, that is fairly obvious, isn't it?

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A. That's right.

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Q. Did you ever at any point in  
time confront these officers as to why they were  
focusing you and your sampling and your testing of  
those samples, why they were focusing you on  
digoxin?

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A. I am not sure whether I would  
use the word "confronted", but we have many  
discussions and I am sure I was briefed in on  
aspects of their investigation which were relevant to  
digoxin analysis. As I recall it there was prior  
knowledge of digoxin, the possibility of digoxin  
involvement.

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THE COMMISSIONER: Yes, Mr. Marshall?

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MR. MARSHALL: As I understand,

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Mr. Commissioner, and I hesitate to rise, I thought we were going to try to departmentalize the whole proceeding.

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THE COMMISSIONER: Yes, we might be into the second, or perhaps third phase of the investigation, if you think it is on the first phase carry on for a while, bear that in mind, that's all.

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MR. SHANAHAN: As I say, Mr. Commissioner, my concern was we were right in on digoxin and maybe there is something I missed as to where you got started in digoxin. It seems to me people came to you and asked you to test for digoxin?

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THE WITNESS: Yes.

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MR. SHANAHAN: Q. And you weren't involved in any of the background decisions with respect to why it was digoxin as opposed to any other toxic drug that may be present in the Hospital.

A. I may have been, and I probably was.

Q. Did you then test for - I don't really need to know what they were, but did you then test for other drugs besides digoxin in these samples?





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A. Well, as I recall it again we tested at least one baby for other drugs.

Q. In at least one?

A. That's right in at least one as I recall it.

Q. Would it be fair to say in the others you didn't, you tested exclusively for digoxin?

A. The subject of refreshing my memory as I go through all those 24 babies, but in at least one we tested for other drugs.

Q. Just a few questions with respect to factors that may influence the reading. I think you said that because digoxin is metabolized to a minor extent in practical terms unless you had severe renal failure you felt the readings you would get from the body were accurate. You felt that renal failure perhaps was a complicated factor insofar as the bodies ability or lack of it to get rid of digoxin.

A. I believe I was referring to the accumulation of metabolized <sup>tes</sup>~~zed~~ that is as a result of renal impairment.

Q. What I am asking you then, if a child was in severe renal failure over an extended







1  
2 period of time, do you know, is it your expertise  
3 to answer this question; do you know whether in  
4 fact that would influence the accuracy of the  
5 digoxin reading that you would get?

6 A. Before I can answer it I am  
7 not sure what you mean, accuracy with respect to  
8 what?

9 Q. Your digoxin reading.

10 A. By what technique?

11 Q. By the RIA technique.

12 A. RIA technique? If a child  
13 was in renal failure it is possible there would  
14 be an accumulation of metabolites which are known  
15 to cross-react to some extent with the RIA procedure.

16 Q. Would that then not be something  
17 that you should know, or something that should be  
18 provided to you before you could really comment on  
19 the reading that you got, whether this child was in  
20 severe renal failure over an extended period of time?

21 A. I believe I did have that  
22 information at some point.

23 Q. What about the masking of some  
24 drugs on another drug? If a diurectic drug would  
25 cause elimination of drugs from the body and if a  
person was to administer an overdose of digoxin but







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also administer a diuretic, could that diuretic in some way confuse your ability to give us a reading of how much digoxin was in the body at the point of death?

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A. That is a very general question.

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THE COMMISSIONER: Would it not depend on the type of diuretic?

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MR. SHANAHAN: Q. Well, in general a diuretic that would cause the expulsion of waste material, that would assist the kidneys in the expulsion of waste material, could that not, if it was administered at or around the same time as the overdose of digoxin subsequently mask the digoxin levels that might have been in the blood at the point of death, or can you not answer that?

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A. I don't believe I can answer that, I don't really understand.

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Q. Finally then, in terms of samples that you might have got from exhumed bodies, again would the police officers provide you with the samples?

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A. As I recall it as a rule this is what happens, the police officers bring the samples.

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Q. Were you aware that the bodies





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were going to be exhumed?

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A. Again, we had quite a few  
bodies, generally yes, but not in all cases.

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Q. Did you direct them to where  
you wanted, obviously it would seem to me now that  
we are not talking blood samples we are talking  
tissue samples.

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A. Yes.

Q. Did you direct them as to  
where you wished those tissue samples from?

A. I had discussions about it  
with the pathologists as well as with the police  
officers.

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Q. Did the pathologist make the  
decision as to where the best sample would come for  
testing purposes, or did you make that decision?

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A. I don't know, I don't know  
who makes the decision, some consultations between  
myself and the pathologists.

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Q. We have heard about blood  
samples from the brain, and the heart and this  
type of thing, where was it felt the tissue sample  
should be taken from the bodies of exhumed infants  
to provide you with the most accurate digoxin reading  
after death?





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A. I could answer that from my general recollection but it is really something which I was thinking we would discuss at the latest stage.

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THE COMMISSIONER: The question isn't where they did take it from, the question was where was the best place, can you answer that?

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THE WITNESS: There were a number of occasions that I discussed with pathologists, I suggested a source of any fluid or blood.

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THE COMMISSIONER: Any fluid?

THE WITNESS: Yes, or blood that might be present, body fluid or blood. I suggested heart tissue and some of the regions of the heart tissue that I felt should be collected. I suggested lung tissue and I think those were also suggested, the presence of vitreous humor should be available.

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MR. SHANAHAN: Q. Vitreous humor, is that the eye?

A. That is the fluid in the eye, that's right.

Q. Was it a concern of yours --

A. As well as some other tissues because we felt once the exhumation is carried out we might get other tissues as well and study the







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2 distribution. This was something really that has  
3 not been done before and was something which, that  
4 we had no other experience to draw on, no experience  
5 of anybody else to draw on.

6 Q. That was going to be my next  
7 question and Mr. Lamek can curtail me here if I'm  
8 getting into that further area that I have no desire  
9 to. Did it not concern you then that obviously you  
10 were now into an area that was going to be at least  
11 somewhat confused by the general decomposition  
12 process and also by the embalming process, and you  
13 were really headed into an unknown region, is that  
right?

14 A. That is right.

15 Q. How can you be confident that  
16 the digoxin readings that you got from the bodies  
and tissues of exhumed babies are accurate?

17 A. Are what?

18 Q. Are accurate in view of the  
19 decomposition and the embalming process they had  
20 undergone?

21 MR. LAMEK: Mr. Commissioner, at  
22 that stage are we not getting into the interpretation  
23 of particular results which is the subject matter of  
24 later evidence?  
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THE COMMISSIONER: Yes, but is it  
a general question, is this not a general question?

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MR. LAMEK: I think it was  
expressed in terms of the measure of confidence  
one could have with results obtained from the  
exhumed babies.

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THE COMMISSIONER: Mr. Shanahan  
may be asking whether there is a difference between  
exhumed, there is a difference in the reliability of  
tests of exhumed babies and on those that were not,  
and if that is so I think it is a legitimate question,  
if that is the question I have no problem, I don't  
know if that is the question.

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MR. SHANAHAN: That is the thrust  
of the question.

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THE WITNESS: Would you repeat that  
question again.

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MR. SHANAHAN: Q. Yes. The  
reliability of the test you have gone through here  
for us with respect to blood and tissue before  
death and after death, but my concern as I heard your  
evidence here was the reliability of those tests  
you mentioned with respect to a body that has already  
been embalmed and has obviously, because of the fact  
it has been dead some time there has been some





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time there has been some decomposition, this is  
a new area you have just said for you.

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A. Yes.

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Q. And I am just here - I am not confident and I am wondering why you are confident that your readings on exhumed body tissues --

THE COMMISSIONER: If indeed he is. If he is confident. I haven't heard that he was that confident, but we will --

MR. SHANAHAN: I think he used the expression - I have in my notes here that you used the expression you were reasonably certain --

THE WITNESS: Yes.

MR. SHANAHAN: Q. And reasonably sure. They seem to be the catch phrases you had about your testing methods.

A. Yes.

Q. But I am saying --

A. Reasonably satisfied.

Q. All right. Reasonably satisfied.

Can you be reasonably satisfied with respect to the accuracy of those tests that you have outlined for us with respect to tissues of exhumed bodies?

A. Well, yes, I am as far as the identification of the presence of the drug. I am satisfied within what I believe is reasonable scientific certainty that it is a true identification.







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With respect to the other, to the other, to the interpretation of the result, of course this is a different proposition.

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MR. SHANAHAN: All right. We will leave that interpretation until later then. Thank you.

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THE COMMISSIONER: Mr. Tobias?

CROSS-EXAMINATION BY MR. TOBIAS:

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Q. Mr. Cimbura, several times in your evidence in chief and in cross-examination you pointed out a distinction between obtaining a reading of digoxin levels and the interpretation of that reading.

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Are you aware of who it was who aided the police in the interpretation of the readings which you obtained?

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A. Well, I would like to believe that I aided them. As well as other people, yes.

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Q. All right. There were other people involved in the interpreting process other than yourself?

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A. That is right.  
Q. Right. And would those people have been on the staff of the Centre for Forensic Sciences?

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MR. LAMEK: This is a long way from methodology, Mr. Commissioner.

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THE COMMISSIONER: Well, I don't know,  
it certainly seems to be getting into the --

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MR. TOBIAS: I don't --

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THE COMMISSIONER: If Mr. Lamek is  
going to rule us on how we divide this up, it would  
certainly seem to come under his second heading.

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MR. TOBIAS: I don't want to dwell on  
the point. I am hoping that through the answer I get  
I will be satisfied that the questions can be asked  
at a later stage of other witnesses, and I am just  
trying to establish that in this question.

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THE COMMISSIONER: Well, let's have  
the question. I have now forgotten the question so  
let's have that again and we will see ...

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MR. TOBIAS: Q The other individuals  
who were involved in helping you interpret the results,  
would they be on the staff of the Centre for Forensic  
Sciences?

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THE COMMISSIONER: Were some of them?

THE WITNESS: I am sorry, Mr.  
Commissioner, I was not sure whether you wanted me to  
answer.

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THE COMMISSIONER: Well, yes, answer it  
if you can.

THE WITNESS: Of course there are





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individuals, my colleagues in Toxicology at the Centre for Forensic Sciences, but I think what you are referring to is to people outside.

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There was at least one person that I know of who was outside the Centre for Forensic Sciences, and again I am not sure in what interval of time your question is directed to; at the beginning, before the preliminary hearing or after? At what stage and so on?

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THE COMMISSIONER: Well, the answer is some of them were from the Centre for Forensic Sciences. Is that right?

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THE WITNESS: Well --

THE COMMISSIONER: Some of the people that assisted in the interpretation of these results were from the Centre?

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THE WITNESS: If I recall the question correctly, assisted the police, that would sort of leave out --

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THE COMMISSIONER: Just you and the police; there was no one else in the Centre that --

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THE WITNESS: There was no one else in the Centre and there was, depending on the time, at least one person from outside the Centre.

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THE COMMISSIONER: The answer then I







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guess is no, Mr. Tobias.

MR. TOBIAS: Thank you.

Q Now you indicated in chief yesterday that there was a generally accepted therapeutic range which could be expressed in terms of nanograms per millilitre of blood.

Can that generally accepted therapeutic range also be expressed in terms of nanogram per gram of tissue?

THE COMMISSIONER: I thought the evidence was that we did, with tissue, we did express it as per gram, and with fluid we expressed it as per millilitre. Is that right?

THE WITNESS: Right.

MR. TOBIAS: Q Your evidence was that anything up to 4 nanograms per millilitre of blood would be generally accepted to fall within the therapeutic range.

Can we assume from that then that anything up to 4 nanograms per gram found in tissue would also be accepted to generally fall within the therapeutic range --

A. No.

Q -- or would that figure differ when we are dealing with tissue?





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A. There are just two points. First of all this was with respect to young infants, that figure of 3 or 4.

Q. Yes.

A. And secondly, the tissue concentrations would be entirely different, would likely be entirely different. One could call a normal range of concentrations in the tissues, and this would be quite different than for blood.

Q. All right. With respect to testing done on tissue and with respect to the results obtained from testing on tissue, can we say that there is a generally accepted range which would fall within the therapeutic category, or does it depend on where the sample was taken from, what tissue the sample was taken from and other variable factors?

A. One would have to individualize the separate tissue and then based on results published in the literature, and based on my own research, one could give the ranges that are found in different tissues following therapeutic administration of digoxin to people.

Q. Let me be specific. Let me talk about heart tissue taken post mortem on autopsy.

Would you agree with me that on a heart





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sample taken post mortem you would be able to come up with a reading which from the literature and from your own research you would feel confident to indicate that that particular level of digoxin fell within a therapeutic range?

A. I could find a level which may or may not fall into the range that I know it.

Q. All right.

A. The usefulness of the diagnosis let's say of digoxin toxicity from tissue as opposed to blood --

Q. I am trying to ask for your assistance in helping --

MR. LAMEK: Sorry, I don't think Mr. Cimbura finished that answer.

THE WITNESS: Yes, I was going to say something more, that is right.

MR. TOBIAS: Q. Go ahead, please.

A. The usefulness of an interpretation or diagnosis of concentration from a tissue as opposed to blood is in my view much, very much limited, because of considerable overlapping between the ranges found after normal doses and the ranges found after let's say in cases of fatal poisoning, there is a considerable overlap in some tissues.







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So for that reason when I was asked previously the specimen of choice for interpretation was blood; tissues - in tissue the interpretation is much more limited, the usefulness of interpretation is much more limited.

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Q Are you indicating that indeed the interpretation with respect to tissue is much more difficult?

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A That is right.

Q All right. Is there a considerable overlap in between what you would --

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A From tissues alone, yes, it is much more difficult.

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Q I understand that. Specifically with respect to heart tissue is there a considerable overlap in what you would consider a normal or therapeutic range and a toxic range?

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A Yes, there is.

Q Now with respect to the RIA technique and utilizing it specifically on preserved tissue, that is tissue that is aged and has been preserved from autopsy, is there any relationship between the age of the sample of the tissue sample and the accuracy of the reading for digoxin levels?

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A I am not sure I know what you







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mean by "accuracy"?

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Q. Let me clarify it. You talked yesterday about a phenomenon called elevation, and you said that it was generally accepted that digoxin levels in the blood post mortem would be somewhat higher than pre mortem, and then you gave us a number of specifics: the site that the blood was drawn from, the timing of the sample, the amount of digoxin that had been administered.

Is there the same type of relationship with respect to elevation relating to the age of the tissue sample? Would you expect a higher reading on tissue that had been preserved, let's say, six months as opposed to tissue preserved for three months?

A. Preserved with what?

Q. Let's say formaldehyde as an example.

A. What I would expect in a tissue preserved with - well, my experience is with tissue preserved in Klotz solution which contains formaldehyde so if I may answer on that basis?

Q. Yes. All right.

A. On that basis. My experience with that is that the stability of digoxin decreases





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with time and also that the digoxin diffuses from the tissue and goes into the surrounding solution, surrounding Klotz solution which would with time tend to decrease the concentration in, let's say, six months as opposed to three months.

Q. Is it fair to say then that the older the tissue the lower the reading should be, and conversely the higher the reading would be in the fluid?

A. Will you say that again, please?

Q. Yes. Is it fair to say then, can I draw the conclusion that the older the tissue sample is the lower the reading will be in the tissue sample and the higher the reading will be in the fluid sample as the digoxin is diffused from tissue into the fluid sample?

THE COMMISSIONER: It is not a fluid sample it is the fluid, the preservative.

MR. TOBIAS: Q. Or the fluid, the preservative, rather.

A. Referring to Klotz preservative?

Q. Yes.

A. Well, up to some extent I would agree with that. At some time there may be equilibrium established which this process stops. I am not sure ...





L.11

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Q. I see.

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A. But for some time at least I would expect that digoxin would go from the tissue into the surrounding Klotz medium.

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Q. All right. And does your research indicate to you or does it give you any range of when this natural process of diffusion would stop?

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A. Well, we have studied it for some periods of time and I have not refreshed my memory on this aspect. I think I could - there are records available and I could discuss it with more detail when I appear next.

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Q. All right, well, my next

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question was --

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A. But the study was done for  
some time.

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Q. All right. Are you referring

to the study that you agreed yesterday to produce for  
Mr. Lamek?

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A. No, this is a different study.

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Q. This is a different study?

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A. That's right.

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Q. All right. Well, I wonder if

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you could refer to that study and perhaps when you  
come back we can get that question answered.

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A. All right.

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THE COMMISSIONER: I think if you can

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do that, can you?

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THE WITNESS: Well, you know, I came,

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it was my understanding that we may not go into these  
aspects on first appearance and I believe, to some  
extent --

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MR. LAMEK: I thought so too.

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THE WITNESS: Pardon me?

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MR. LAMEK: I thought so too, Mr.

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Cimbura.

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THE WITNESS: I certainly have the

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results of that study available. I would prefer to refresh my memory on that, perhaps if I am allowed to get back to it at the next appearance.

MR. TOBIAS: Q. That's fine. Now, you testified yesterday in cross-examination that levels of digoxin would vary pre and post mortem depending on the site that the blood sample is taken from. Can we take it that that proposition is also true with respect to the site of tissue sample?

A. Would you mind repeating that question again, please?

Q. You indicated yesterday that the levels of digoxin found pre and post mortem would tend to vary with respect to the site the blood sample was drawn from.

A. The post mortem samples would tend to ...

Q. Would tend to vary?

A. Would tend to vary depending on the site collected from, that's right.

Q. Is that also true with respect to the site where tissue samples were taken from?

A. Well, I don't know what you mean, the tissue samples. Do you mean, let's say, with respect to heart? This could vary, for example, from





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my experience, with respect to heart, yes.

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Q. All right. That was my next

question. Would you expect the post mortem reading taken on heart tissue to be higher, for instance, than on liver tissue?

A. After what circumstances, after normal administration, after toxic administration? I am not sure I know what you are referring to.

Q. All right. Well, let's talk about after a normal therapeutic dosage. Would you expect the concentrations in the heart tissue post mortem to be somewhat higher than the concentrations to be found in liver tissue?

A. They could be higher, yes, in some parts of the heart, yes.

Q. All right, you say they could be. But would you say as a general rule they would be?

A. Well, there's such a range of values that one can obtain. Let's say in the ventricular part of the heart, in the ventricular muscle.

Q. Yes?

A. Yes, as I recall it, I would expect to find higher values in the same person than in the liver tissue.







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Q. All right. Now, in answering Mr. Shanahan's questions, you indicated that you would be fairly confident in the readings that you obtained from exhumed tissue, but the question of the interpretation of those readings was another matter. Was that statement in any way related to what you have previously told me about the natural diffusing process?

A. This may be one of the factors involved. Your question now is with respect to embalmed tissue, is that right?

Q. Yes, that's correct.

A. This may be a factor, and there are other factors involved.

Q. Specifically what I want to know is this. Assuming that there is no embalming, as the tissue decays after death, does the tissue excrete or throw off digoxin or will it stay in that tissue?

A. Well, I know it stays in it for some periods of time because we have, what I believe identified it in the tissue. Does that answer your question?

Q. Well, partly. What I'm getting at is this. Would you say that with respect to exhumed tissue it is again fair to say that as that tissue ages with the length of time increasing, in







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other words after death, you would expect the digoxin reading to become somewhat lower until that process of diffusing stopped?

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A. Well, this was referring specifically to tissue --

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Q. Which was preserved?

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A. -- which will be preserved in Klotz solution.

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Q. All right. Now, I am asking you to address that same issue with respect to tissue that is not preserved.

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A. It is not in any medium, just a tissue by itself?

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Q. That is correct.

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A. Yes.

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Q. Will that tissue retain digoxin or will the digoxin be diffused out of that tissue by some process?

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A. Well, it will retain digoxin, from my experience, for some time.

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Q. All right. And with respect to the study that you referred to before, after you've had an opportunity to read that and refresh your memory, would that help you estimate that period of time for us?

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A. No, I think in an embalming situation there are many other factors that have to be taken into account. This is only one of the factors.

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THE COMMISSIONER: Surely the whole tissue disintegrates, does it not?

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THE WITNESS: Yes, some of it. It depends on the tissue and so on. Some tissue may decay considerably but still we have found digoxin in it. How it reflects the amount that was in the tissue, let's say at the period soon after that, of course this is one of the problems and this is one of the problems with the interpretation.

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MR. TOBIAS: Q. And that is in fact a matter for interpretation?

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A. Pardon me?

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Q. I say that is in fact a matter for interpretation of the reading?

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A. That's right, this is one of the factors which make the interpretation very difficult and, in my view, in many cases inconclusive.

MR. TOBIAS: Thank you.

THE COMMISSIONER: Thank you, Mr. Tobias. Mr. Manning, I won't ask you to start now but perhaps you could tell us how long you will be?





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MR. MANNING: Three-quarters of an

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hour.

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THE COMMISSIONER: Yes, Mr. Lamek,

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have you any thoughts on how long you will be?

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MR. LAMEK: Mr. Commissioner, I suspect

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I will be 30 to 40 minutes in re-examination.

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THE COMMISSIONER: I think then we can

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dispense with any further witnesses today.

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MS. CRONK: I agree.

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THE COMMISSIONER: Yes, all right, we

will rise until 2:30.

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--- Luncheon adjournment

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--- Upon resuming at 2:30 p.m.

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THE COMMISSIONER: Mr. Manning?

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MR. MANNING: Thank you, Mr.

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Commissioner.

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CROSS-EXAMINATION BY MR. MANNING:

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Q. Mr. Cimbura, the Centre for

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Forensic Sciences in Toronto where you are presently  
employed was previously known as the Attorney General's  
Laboratory, is that not correct?

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A. That's correct, sir.

11

Q. And that Centre is set up in

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order to do the kind of analysis that you've described  
in the last two days, among other things?

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A?

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Q.

When the police came to you with  
some samples for you to analyze, naturally they  
discussed what they thought <sup>was</sup> of the kind of analysis  
that should be carried out and you yourself then, sir,  
made a determination that an analysis of the samples  
in order to determine whether there was a content in  
those samples of digoxin was required, is that correct?

19

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A. Well, they didn't discuss with me

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the kind of analyses, they discussed with me the drug  
for which the analysis should be carried out.

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Q. I understand that.

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A. But not the kind of analyses, I

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don't believe, was discussed with me by the police,  
not at least that I can recall.

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Q. And it would have been impossible

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to say or to determine what substance you were looking  
for. <sup>if no -</sup> ~~no~~ one had said to you look for a specific

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substance; in other words, if they had brought a

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sample to you and said, what's in this sample of blood,

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you possibly, given an unlimited amount of time and an

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unlimited amount of resources, could have found out

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what was in the sample of blood?

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A. Well, it would be much more

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difficult to detect in a limited sample and so on a

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drug without prior knowledge of what one is looking  
for.

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Q. Exactly.

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A. It is standard procedure in

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toxicological analysis is that it helps very much

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to know what the suspected drugs are so the analyses

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can be specialized and optimized.

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Q. And narrowed down?

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A. And narrowed down, that's right.

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Q. And indeed in this case you were

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asked to look into the samples that were brought to you

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to determine whether there was digoxin in those samples

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and, if so, how much; correct?

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A. I believe so, yes. I was asked to analyze digoxin, which naturally it goes with it to find out if it's there and how much is in there.

Q. Certainly. And at first instance, as we have already heard, you declined on the basis that there was not <sup>an</sup> ~~the~~ established procedure at the Centre for Forensic Science in order to carry out such a test?

A. That's correct.

Q. All right. Even though there was the equipment to carry out the analysis on various substances in order to determine whether they contained other substances?

A. Yes, other equipment capable of doing other drug analyses, even carrying out digoxin analyses. But the procedure for utilizing this equipment, the evaluation was not available.

Q. And I believe you indicated yesterday that you had learned about digoxin certainly as far back as when you were in school?

A. That's right.

Q. And indeed the literature would seem to indicate that digoxin, being a derivative of digitalis, has been known to effect the reaction or affect the action on the myocardium in the heart for







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quite a number of years?

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A. Yes.

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Q. And, indeed, the literature also

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indicates that digoxin has been used by various

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African and primitive tribes many hundreds of years  
ago as a poison?

7

A. Well, that may have been in the

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form of crude plant products, rather than as opposed

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to specifically digoxin.

10

Q. Certainly, but the digitalis

11

itself had been used as a poison?

12

A. Yes, I recall from my history

13

days, I don't know exactly how long a time ago it was,

14

that's right, yes. Quite a long time ago, that's right.

15

Q. And, indeed, it could be said

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that as a scientific matter a derivative of digitalis,  
if administered at too high a dose could be a poison?

17

A. Yes.

18

Q. So, it became important, once

19

the decision was made for the Centre for Forensic

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Sciences to analyze the substances in order to find

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whether there was digoxin for the Centre to also find

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how much there was in each of the samples?

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A. Generally speaking that's right,

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yes.

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Q. Right. Now, in order to start the process of establishing the procedure to find out whether the unknown substance in the sample that was given to you was digoxin, you had to sit down and research the literature first in order to find out whether there was available elsewhere an established procedure for testing for digoxin?

A. I agree, I sat down and reviewed the literature mainly for that sort of information and also information which would enable me to select an appropriate procedure to study.

Q. Exactly. And the two procedures that you decided upon, after the end of your research, were radioimmunoassay and the other test that we've heard about, the pressure -- let me get that -- the high pressure liquid chromatography?

A. That's correct, sir.

Q. And, as well, you tried gas chromatography?

A. Gas chromatography coupled with mass spectrometry.

Q. Right. I will come to those in a moment. But is it fair to say, sir, that those tests are referred in the Forensic Science literature, referred to as specific tests?





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A. The two tests combined or each one of them or what?

Q. The two tests combined.

A. Well, I'm not sure whether I have seen reference to them as a specific test because there have been relatively very few reports utilizing these two techniques in the forensic literature together. So, I cannot answer your question. The combination of the two in forensic literature, the combination of the two techniques is not mentioned. There are very few reports in forensic literature.

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Q. So that was really a procedure that was unique to the Centre of Forensic Sciences?

A. Well, there was some references in other forensic literature to the use of HPLC.

Q. Along with the RIA method?

A. Yes, I believe so and various modifications, yes.

Q. Now in order to find out what procedure to follow, did you determine what manufacturer supplied the digoxin to the children at the Sick Children's Hospital?

A. I don't believe at that time, no.

Q. Are you aware, sir, some of the literature seems to indicate that important differences in the bio-availability of the digoxin in different preparations depends on which manufacturer manufactured it?

A. Which manufacturer?

THE COMMISSIONER: I am sorry, what was that again?

MR. MANNING: The bio-availability?

THE COMMISSIONER: Bio-availability?

MR. MANNING: Of digoxin, different preparations vary according to the manufacturer.

THE COMMISSIONER: Can you help me as to what it means.







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MR. MANNING: It is the living availability of digoxin in the particular preparation, the percentage varies or the purity may vary according to the different manufacturing procedures. Are you aware of that, sir?

THE WITNESS: I recollect some literature that possibly referred to this phenomena with respect to that.

MR. MANNING: Q. But that made no difference to the tests that were carried out by the Centre?

A. Well, this is something which I would expect, there may be some differences in the characteristics of RIA depending on different manufacturers that made a difference in my selection.

Q. I wasn't asking you about the selection with respect to the RIA, I was asking about the manufacture of digoxin generally?

A. Well, automatically the manufacturer will reflect on the RIA, they are commercially available from the manufacturers. So if you have reservations about the manufacturer you would have reservations about the RIA.

Q. How many manufacturers of digoxin are you aware of that exist in North America?





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A. I haven't counted them, sir.

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Q. Are there a lot?

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A. There are some, yes.

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Q. Would there be more than half a dozen?

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A. There could be, yes.

7

Q. Or a dozen?

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MR. LAMEK: He said he doesn't know,

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Mr. Manning.

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MR. MANNING: Q. How many manufacturers

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of the kit involved in the RIA process are there?

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A. I believe that is what you just

13

asked me, sir, unless I am wrong?

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Q. Perhaps I haven't made myself

clear.

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A. Perhaps I am not clear.

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Q. Is there a difference between

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the manufacturer of digoxin on the one hand and the

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manufacturer of the kit in the RIA process on the

19

other?

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A. Oh, I see, I am sorry. I didn't

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understand your question that way and I apologize, and

22

could we go back to your question from that point of

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Q. All right. My first question

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was, how many different manufacturers of digoxin are  
there in North America today?

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A. The digoxin standards you mean  
purchasing the pure drug digoxin?

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Q. The pure drug, yes?

7

A. I don't really know. I know of  
at least one, at least two, and there may be more.

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Q. And how many manufacturers of  
the kit of the type that you used in the RIA process  
from the Beckman Company are there in North America  
today?

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A. How many manufacturers of the  
same kit that I have purchased?

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Q. Yes, the same or a similar type  
kit?

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A. Well by similar meaning just  
that form of RIA, is that what you mean?

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Q. Yes.

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A. There are quite a few, I don't  
know exactly the number.

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Q. Is there any reason Mr. Cimbura  
why you picked the Beckman kit as opposed to some  
other kit?

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A. Yes, there was some reasons. The  
particular kit was described in the literature, in the

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forensic literature in the reports prepared by some colleagues that I know of. I have read the report, and one of the characteristics that I was interested in from their report was that this particular RIA, readings, for example, did not cross-react with formaldehyde, and this was one reason, as well as their report that they found it very satisfactory for working with fresh tissue specimens. That was one reason why this particular kit was chosen after reviewing literature.

11

Q The Beckman kit that was used --

12

A There was another reason.

13

Q I am sorry, certainly.

14

A It did mention other reasons but

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one reason I just thought of right now is this was, the system is described as a double antibody system and this was alluded to in the forensic literature and this was of interest to me because I believed it facilitates better analysis.

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Q Does it also give a more sensitive result?

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A I don't believe more sensitive, a more accurate result, more precise result perhaps is a better word to use.

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Q And that particular RIA test

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BB.6

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2 that you carried out, generally, was that carried out  
3 subsequent to the other test that was made, or prior  
4 to? In other words, which test did you do first, did  
5 you do the high-pressure liquid chromatography test  
6 first, or the RIA test first?

7 A. As I recall it, and as I believe  
8 I mentioned it previously my recollection is we  
9 started with the RIA test, the evaluation of the RIA  
10 test first and then proceeded at some later stage  
11 to the evaluation and development of the HPLC. I  
12 believe we have concluded before and I will refresh  
13 my memory on that and bring it up at a later date,  
14 but that is my recollection.

15 Q. And certainly it would make  
16 better scientific sense would it not to have two tests  
17 instead of one?

18 A. It would make, it would be more  
19 logical from a forensic point of view. As I mentioned  
20 again previously it is normal procedure to use  
21 different tests for identification.

22 Q. And so as well as utilizing the  
23 HPLC test in a number of ways, you also used it to  
24 confirm the RIA test?

25 A. So to speak, yes.

Q. So that you had two tests that if





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one of them was out of line that would indicate there might be something wrong with the other test?

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THE COMMISSIONER: My understanding was that you did the RIA test and then you did the HPLC test in order to check the validity of the RIA test, and then having determined what the HPLC test showed you went back and did another RIA test, have I got that wrong?

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THE WITNESS: Slightly, I believe, if I may revise it slightly, the second RIA is a means of detection following the HPLC test.

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THE COMMISSIONER: That is what I meant, isn't that the procedure, RIA, HPLC, RIA?

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THE WITNESS: That is correct.

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THE COMMISSIONER: You said that and then you questioned it, have I got that right?

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THE WITNESS: That is the sequence, that's right.

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MR. MANNING: Q. So in effect then you had three tests for each of the samples, the RIA test, the HPLC test and then the RIA test again?

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A. If you want to call it that, yes, I call the HPLC and the subsequent RIA, somehow I referred to it as part of the same procedure, but I guess you could call it another test, yes. As a





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matter of fact in some cases we have done another even test than that, another RIA before we start the initial RIA, and then another RIA before we even started with the HPLC, and then still another RIA after that. It is a question of semantics I suppose how many different tests you want to call it.

Q Well, it is more than that, isn't it, Mr. Cimbura, it is also a matter of attempting to achieve the maximum degree of scientific accuracy?

A Well, that is right, sir, that was our intention and that is what we tried to achieve.

Q And indeed the literature with respect to both tests suggests that one test should be confirmed by another test, which is exactly what you did or sought to be confirmed?

THE COMMISSIONER: The difference, Mr. Manning, as I understood it, the HPLC by itself means nothing, all it does is take it in some way it gives you a refined sample, if you like, so you can do the RIA test properly, isn't that right?

THE WITNESS: That is correct.

THE COMMISSIONER: You correct me if I am wrong, but the HPLC is not a test in itself, all







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it does is refine the sample to allow you to do a proper test on the RIA, am I right, or am I wrong?

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THE WITNESS: Well, personally, I regarded the HPLC-RIA as one test.

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THE COMMISSIONER: If you just forget about the RIA, throw it out the window for purposes of this, and just do the HPLC test, that will do nothing except produce a purer sample of digoxin, isn't that right?

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THE WITNESS: That's right, and the way we used it it wouldn't give results by itself.

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THE COMMISSIONER: That's what I thought. It is not really an additional test it is a part of the RIA test to make it better. I have said that, and if I am wrong I would like you to correct me.

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THE WITNESS: In my view I regarded the HPLC followed by RIA as one procedure.

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MR. MANNING: Q. If I can break down the one procedure into several parts. The HPLC test, would you agree is a screening procedure used to separate and tentatively identify a variety of substances?

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A. It is a separator procedure I think as I would refer to it.

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Q. To separate and tentatively identify?

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A. And with some drugs it may be  
used to tentatively identify, that is right.

Q. And ---

A. And not with digoxin, as far as  
the tentative identification because of the various  
technical problems and that is the reason why we have  
resorted to RIA after HPLC.

Q. But dealing first with the HPLC  
test you indicated yesterday it was a column test,  
or a test that utilized pressure columns, correct?





CC/EMT/ak

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A. One essential component is a  
chromotographic column, that is right.

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Q. And can you get a graph as a  
result of the utilization of that equipment?

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A. You can get a graph, yes.

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Q. Did you in fact get graphs in  
the samples that you tested with respect to this  
investigation?

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A. We got graphs in respect to  
calibration curves that were prepared on that, and  
information relevant to calculate the concentration  
of digoxin in most cases. In some cases part of  
our research operation we did get different kinds of  
graphs.

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It is hard for me to define what is  
actually a graph and what is not a graph. Some  
record - the record is available. The records  
produced.

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Q. You have those records with  
respect to each of the tests?

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A. Yes, we should have them, yes.  
All these tests, yes.

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Q. And they can be produced when  
you discuss each of the individual tests?

A. They can be produced. It will





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mean bringing, you know, to the hearing a large  
volume of data, an awful lot of data.

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Q. I'm sorry, what kind?

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A. Quite a lot of data. I know  
these records which have been produced in the  
course of the investigation are physically a very  
large volume of data.

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MR. MANNING: Perhaps, Mr. Commssioner,  
they could be made available to Mr. Lamek and then  
counsel could examine them to see if any one of them  
ought to be produced. In other words, just to make  
them available for examination.

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THE COMMISSIONER: I would much  
rather make them available for examination but my  
horror is that we are going to turn this Inquiry  
into an examination for discovery and that is what  
I don't want to happen.

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I want cross-examination if possible  
to be based upon information of some kind. It may  
be - it may be that the best thing to do would be  
to let Mr. Manning loose with his documents to see  
what he can do, but I really don't want it - unless  
you have got some ground to satisfy me what you are  
heading for, I don't want to have each document  
investigated in the hope of finding something wrong







1  
2 with it, because that way is another way we would  
3 be here forever.

4 We don't have examination for  
5 discovery in an inquiry. I know that this pursuit  
6 of absolute truth will take us longer than I am  
7 prepared or the public is prepared to tolerate. So  
8 we have - we may have to use some kind of discretion,  
9 that is all.

10 MR. MANNING: Well, I would like an  
11 opportunity to review the material.

12 THE COMMISSIONER: There is no  
13 reason why you can't go to --

14 MR. MANNING: All right.

15 THE COMMISSIONER: -- to any place  
16 and investigate any document that you would like,  
17 but all I would ask is when you are questioning on  
18 some document don't just question to find out - I  
19 know you won't do this - just to find out if there is  
20 something wrong, but once you believe there is  
21 something wrong to demonstrate that it is wrong.

22 I know we are just at the beginning of  
23 this Inquiry and there is going to be a problem here,  
24 but please remember it is not an examination for  
25 discovery.

MR. MANNING: I have no intention





CC4

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of using this Inquiry - it never entered my mind;  
there is no lawsuit in which I am involved --

4

THE COMMISSIONER: No, no, I'm sorry.

5

I am not suggesting that anybody is using it improperly.

6

I am just saying that we can't take the time for

7

an examination for discovery. But I am quite happy -

8

at least I am quite happy; I don't know whether

9

Mr. Lamek is quite happy - to make available to you

10

any of these documents that you can go and look at.

11

And it might even be helpful if you find out that

12

something is wrong to see if we can't clear it

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all up before we even come back here.

MR. MANNING: Thank you.

14

Q. In the test that is being

15

carried out, the HPLC test, there are organic

16

compounds used; is that not correct?

17

A. Well, drugs are organic compounds,  
yes.

18

Q. Yes. There are organic compounds

19

used in this test; is that not correct?

20

A. I suppose. I don't know really

21

what you are getting at but drugs are organic

22

compounds and they are used in standards and so on,  
yes.

23

Q. Well, perhaps part of my

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25





CC5

1  
2 difficulty, Mr. Cimbura, lies in the fact that you  
3 have yet to describe, certainly so that I can under-  
4 stand it and perhaps I am missing something, exactly  
5 how this test works and the kind of equipment that  
6 was actually used in these particular tests.

7 As a general matter, getting back to  
8 what Mr. Lamek started off trying to describe as  
9 the methodology that was gone through - we seem to  
10 have been sidetracked in the last day and a half in  
11 some areas away from actual methodology - I am  
12 bringing you back to actual methodology.

13 In using this particular test you  
14 used certain kinds of equipment; is that correct?

15 A. That is right.

16 Q. And as I understand the way in  
17 which this particular equipment works it pushes  
18 the unknown substance under pressure through some  
19 kind of organic compound and then you measure how  
20 long it takes to get to the other end.

21 A. Of the column, roughly speaking,  
22 yes.

23 Q. Of the column, is that correct?

24 A. That is correct.

25 Q. And there is some method that  
is attached or some machinery that is attached to the







CC6

1  
2 machines that measures how long certain compounds  
3 took to get to the end of the column and then you  
4 refer to certain tables in order to find out what  
5 the compound or solution is in order to find out -  
6 in order to determine - I will go back: in order  
7 to determine that it is the digoxin that is being  
8 pushed through you have to know at the beginning  
9 that digoxin comes through this column in a certain  
period of time.

10 A. That is right. That is called  
11 calibration, yes.

12 Q. Where do you get those calibra-  
13 tion standards? Where did they come from, the  
14 standards that you used for these tests?

15 A. Well, we use two different  
16 standards. One is a tritiated --

17 Q. A what?

18 A. Tritiated digoxin, and this  
19 is used to estimate the time at which we will say  
digoxin will come out from the column.

20 Q. And that particular standard,  
21 dealing with that one alone for the moment, was that  
22 based on your own experimentation, trial and error  
23 method, of trying to determine how long it would take  
24 a known quantity of digoxin to get through the column,  
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or was that based on your reading of literature where some other scientists had performed similar tests over periods of time and come up with standards?

A. The use of tritiated digoxin?

Q. Yes.

A. Well, I think - I am not really sure whether it may have been in the literature. I was aware of it. It may have been described in literature as well. I was aware of it, and the reason why we have used this tritiated standard for this type of estimation, in our estimation, is because it lends itself - the property fractions are collected at the end and counted for radioactivity on a scintillation counter, and thus it can be determined at what time the digoxin comes out from the column.

Q. Is that using --

A. In addition to that we use another calibration with non-tritiated digoxin standards. In other words, with regular digoxin standards.

The calibration curve here is more the regular standard - what I refer to as the standard curve where known quantities of digoxin are injected into the equipment and fractions collected





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from the column at the appropriate time at different concentrations and assayed by radioimmunoassay and to produce a graph with respect to the concentration of the drug that was injected and the reading obtained.

Q. That is using radioactive materials going through the columns; correct?

A. No, the second one is not radioactive material.

Q. And the second one is counted in what way? How do you come up with your counting if you haven't got a radioactive counter?

A. It is carried through a radioimmunoassay which utilizes a radio labelled - ~~iodine~~ <sup>iodine-</sup> labelled digoxin, but the actual drug that is introduced is not radioactive into the HPLC, but it is measured as a regular sample would be measured by radioimmunoassay.

Q. Now as it goes through these columns there is an organic compound in what is called the active phase of the column? Correct?

A. Well I call it a mobile phase. I believe I used the term mobile.

Q. Well, is there not a difference between the active and mobile phase in the HPLC test?

A. I am not sure whether I know







CC9

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what you mean by the term active. If you mean - the mobile phase is the solvent which goes through the chromatographic column.

Q. Yes, at a pre-determined rate of flow?

A. That is right, and then the column in the reverse phase, chromatographic phase coated with another phase, such as a hydrocarbon phase - is that what you were --

Q. Yes.

A. Yes.

Q. The literature seems to indicate that is referred to as the active phase and the other is referred to as the mobile phase.

A. Perhaps. I haven't seen that type of literature but anyway, yes, that phase is there, that is right.

Q. And in the column there are particles of organic compounds; is that correct?

A. Pardon me?

Q. There are particles of organic compounds in the columns.

A. That is right.

Q. All right. What kind of organic compounds were used in the columns in the







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CC10

HPLC test which you ran for these samples?

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A. This was commercially available

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preparation referred to as Microbondapack.

5

Q. And what is the --

6

A. That is a trade name,

7

Microbondapack C18. That is a commercially

8

available preparation.

9

Q. What is it? What chemicals?

10

What organic compound is it? Describe its chemical  
name, please.

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A. It is, as I recall it, it is

12

octadecylsilane, as I recollect it.

13

Q. Octa - can you spell that?

14

A. D-e-c-y-l, silane, s-i-l-a-n-e,

15

is the generic name for it.

16

Q. Have there been any tests to

17

your knowledge from your review of the literature

18

or your experience on the effect of that compound  
on digoxin?

19

A. Well, that particular column

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was described in the literature with respect to

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analyses, with respect to specific analyses for

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digoxin, yes.

23

Q. So that if there was any effect

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on the reading it was taken into account in the set-up

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of the test?

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A. Yes. The normal precautions

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are to run blanks through the column, so that is

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normal precaution in any forensic work that you

6

run blanks through the column to make sure there is

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nothing interfering with the tests.

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Q. Now the RIA test that you

9

used consisting of the Beckman kit, was the test

10

that was used generally - and let's leave the specific

11

test alone for a moment - the ones as set out in

12

this literature that has now been filed as Exhibit 4,

the one that you produced this morning.

13

A. Would you repeat your question?

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Q. There is a procedure set out,

an assay procedure set out?

15

A. Yes.

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Q. In Exhibit 4.

17

A. Yes.

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Q. And do you know whether that

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procedure was the procedure that was followed for

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the analysis or some other procedure?

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A. Well, basically there were some of the modifications I have mentioned before, we used the extraction process.

Q. Micro what?

A. That we used an extraction process before the analysis.

Q. Okay.

A. And also that we used our own standards as opposed to the standards supplied by the manufacturer. There may be some other minor modifications.

Q. And you developed your own standards after experimenting with this subject for a period of months, is that correct?

A. We decided to use our own standards, yes, after some time after initiating the development.

Q. Yes. And you conducted experiments in order to see what standards to use for the RIA test, did you?

A. I really don't know exactly what you mean, sir.

Q. Well, the literature that's supplied with the test kit.

A. Yes.







DD 2

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Q. Sets out, amongst other things,  
an explanation of the test, the principles upon which  
the test is found in?

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A. Yes.

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Q. The materials and reagents  
supplied?

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A. That's right.

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Q. And the assay preparation and  
assay procedure?

10

A. That's right.

11

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Q. It also has standards set out  
in the literature, correct?

13

A. That's right.

14

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Q. All right. You have just said  
that you have used this test kit for the RIA  
procedures for the samples that you were analyzing  
for this investigation, correct?

17

A. With some modifications, yes.

18

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Q. Yes, with some modifications.  
You used the test kit but you didn't use the standards  
that are formulated for that kit, correct?

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A. That is correct.

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Q. So, you must have used your own  
standards developed within the Centre for Forensic  
Sciences itself, correct?

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DD 3

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A. Well, standards are not developed, sir.

Q. How do you find standards, do you do it by experiment?

A. No, standards are either provided or purchased from people who produce the standards.

Q. Like computer software?

A. Yes.

Q. You purchased standards for use in the RIA test from whom?

A. From, as I recall it, Sigma Company.

Q. Sigma?

A. That's right.

Q. S-i-g-m-a?

A. That's right, sir.

Q. And where are they located, sir?

A. I don't recall right now.

Q. Is it a Canadian company?

A. It may be, but I don't recall specifically.

Q. Were there any other standards that were purchased besides the standards from the Beckman Company and the Sigma Company?





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DD 4

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A. There were standards of

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metabolites of digoxin and they were obtained I

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believe rather than purchased from another company.

5

Q. And what company was that, sir?

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A. I should remember because I was

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very grateful to them for being able to supply this,

8

and I have that information available, it is just not

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Q. Perhaps you could supply it at

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another stage. We'll move on. The standards that --

11

A. I will have to put it down so

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that I have that information.

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THE COMMISSIONER: You see, Mr.

14

Manning, what my problem is with that. It may be that

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you have reason to suspect that the standards were

16

inaccurate. Is that what the purpose of this

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MR. MANNING: I don't know, I don't

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have any --

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THE COMMISSIONER: You see, this is

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my problem. If it's going to be an examination for

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discovery we'll be here forever and if you think there

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is something wrong with the standards, if you have

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some evidence to the effect that there is something

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wrong with the standards, I would be delighted to

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pursue this, but if it is merely a question of checking out the standards, if we're going to check out everything that is done by everybody, we are never, never going to get out of here.

MR. MANNING: But how are we to know, Mr. Commissioner, exactly what was done and be able to, at a later stage, certainly not through a discovery process in the courtroom, in this room, but certain if I know the tests that were used --

THE COMMISSIONER: I am happy to give you as much time that you and Mr. Cimbura can afford, but I would like you please, if you have some suspicion, if you think it is wrong, if you know it is wrong, if you want to get some of those facts out, that's fine, but if it is merely to discovering how it's done, we can't take the time to take a course in pharmacology. We just can't do it, we will never never come to an end.

MR. MANNING: Well then, perhaps the solution to this problem could be if Mr. Lamek and Miss Cronk could --

THE COMMISSIONER: Well, I can't afford all of their time either, you know. They have a lot of work to do around here.

However, I was thinking really seriously







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of Mr. Manning investigating this problem for himself to find out and then if you find out there is something wrong by all means bring it up. Do we have to do it here, that's all.

MR. MANNING: I have no objection to sitting down with Mr. Cimbura and finding out exactly what notes he's got and what experiments he's conducted.

THE COMMISSIONER: Well then, I would be delighted if you would do that somewhere.

MR. MANNING: Fine.

THE COMMISSIONER: Somewhere other than here and then if you want to bring him back if you're convinced there is something wrong with the system, that the whole thing is wrong from beginning to end or there is something wrong somewhere, then let's do it. But if you're just going to find out exactly what has taken him years to discover, we are never going to end. That's all.

Now, you understand what my concern is? All I ask you is to consider the concern and I know what your concern is, you want to get the absolute truth, as I have said before.

MR. MANNING: I want to know the facts on it.





DD 7

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THE COMMISSIONER: That's right.

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MR. MANNING: And the only way so far that we've been able to determine the facts is through Mr. Cimbura.

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THE COMMISSIONER: Now, I invite you to go with Mr. Cimbura to his headquarters to go through anything you want there, discover what you want there and then, if need be, we'll have him back for cross-examination. But please let's not take our time to try and go to get ourselves in a position where we can go into competition.

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MR. MANNING: I don't want to be in competition but I did want to find out what he did because I haven't been supplied with any materials as yet which indicate to me exactly what procedures he followed, what standards he used to the full, and what papers he referred to, for example.

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THE COMMISSIONER: All right.

MR. MANNING: I have no objection to doing it outside this room. I don't want to waste your time and I would be pleased to take you up on that suggestion so long as Mr. Cimbura and the Centre for Forensic Sciences co-operate, I would be glad to attend there.

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THE COMMISSIONER: Within certain





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limits I imagine, if they find it's taking up too much time they will complain to me and I will have to discuss it with you. But if in the meantime I would ask you, have you any objection to this procedure, Mr. Lamek? I don't see happiness written all over your face.

MR. LAMEK: Well, Mr. Commissioner, obviously I share your concern. I find it rather astonishing that we've taken two days with Mr. Cimbura, although I understand the complexity of the evidence. The necessity to probe in the way that's been suggested is, well, perhaps a little surprising to me, but then I'm very easily surprised.

The only thing that concerns me, Mr. Commissioner, is your very generous offer of Mr. Cimbura's time and I don't know how readily he will be able to make himself available with the best will in the world.

THE COMMISSIONER: Well, let's experiment with it. Mr. Cimbura, you are not necessarily to devote your full time because I think that the Government has use for your time as well. But if you could assist Mr. Manning to describe in detail what your procedure is and to answer his questions, do you think you could manage to do that?







DD 9

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How long do you think it would take you?

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MR. MANNING: I have no idea, I don't know what he did and I don't know the papers he relied on and I would love to review them.

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While we are on the topic, Mr. Commissioner, I should raise it at this point in light of your comments, I am going to have the same problem with respect, for example, the police with respect to other technical witnesses.

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THE COMMISSIONER: Can we please wait for that. That is several months away, several months away.

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MR. MANNING: Well then, I have the same problem with respect to the other witnesses. For example, the witness that is coming from Vancouver, I don't know whether he's going to refer to anything other than the published paper. If he is, if he's relied on it, if there is data, then perhaps we could be supplied with it so we won't take the time in this hearing. Otherwise, if we can't do it one way or the other, then I can't see, and maybe I'm being obtuse, but I can't see how we're going to find out exactly what happened.

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THE COMMISSIONER: Well, I think you understand -- Yes?





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MR. MARSHALL: I am sorry to interrupt you. The Centre for Forensic Sciences is an agency responsible to the Solicitor General for the Province of Ontario. Perhaps Mr. Manning and I can have a discussion afterwards and perhaps more ready access to some response to his concerns can be arrived at without having the matter debated in extenso here.

THE COMMISSIONER: I would be grateful if you could do that, Mr. Marshall, and if we could get that problem solved. We've already been told that Mr. Cimbura is coming back. If you have something that you know or suspect to be wrong with this procedure by all means cross-examine now. If not, wait until you've had your private investigation and then cross-examine him.

MR. MANNING: All right, I would be glad to wait and I am going to adjourn my cross-examination at this time on that understanding.

THE COMMISSIONER: Well, you're not adjourning, you are going to start again.

MR. MANNING: All right, I will start again but after we've had an opportunity to examine --

THE COMMISSIONER: But I want to exact a promise from you, and you don't need to give it if you don't want to, that you will ask questions only





DD 11

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2 about the matters that after your investigation you  
3 are suspicious about and we can leave aside those that  
4 you find to be in order.

5 I don't want an examination for  
6 discovery, we just haven't got time, that's all.

7 MR. MANNING: But with the greatest  
8 of respect, there's a difference between an examination  
9 for discovery and an inquiry in order to find out  
exactly what happened.

10 THE COMMISSIONER: Yes, all right.

11 MR. MANNING: The background material  
12 that I have been able to read so far, given the limited  
13 amount of time, indicates that there were a lot of  
14 areas, for example, at the preliminary hearing which  
15 were not gone into which, for reasons of the narrow  
parameters of that inquiry, could not be gone into.

16 THE COMMISSIONER: Yes.

17 MR. MANNING: Or for whatever reason  
18 Counsel for the Crown or Counsel for the Defence chose  
19 not to go into. For you to say, sir, that I have to  
20 have, first of all, knowledge of some incorrect  
21 procedure, and I use that as an example, before  
22 examining on it, presupposes I know from before the  
23 witness gets in the witness box what the witness has  
24 done, no matter what the area of inquiry is.  
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THE COMMISSIONER: I have solved that problem for you now by consultation with Mr. Marshall and Mr. Cimbura.

MR. MANNING: Fine.

THE COMMISSIONER: Try it.

MR. MANNING: I certainly will.

THE COMMISSIONER: Let us know what happens.

MR. MANNING: Thank you.

THE COMMISSIONER: All right. Did I miss anyone in this? I think not. Mr. Lamek?

MR. MARSHALL: I should perhaps tell Mr. Manning that I charge a fee for this service!

THE COMMISSIONER: Yes, I'm sure you do and I'm sure you give it away to some ~~noteable~~ charity as well.

All right.

RE-DIRECT EXAMINATION BY MR. LAMEK:

Q. Mr. Cimbura, it's been a long tiring time I am sure but the circles come around and just a couple of things that I want to clear up if I may.

First, can we deal with this question of standards? Obviously the term means different







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things in lay language to that which it means in your business and trade. Do I understand you correctly, Mr. Cimbura, that when you refer to a standard you mean a standard preparation with a known concentration of the drug in issue in it which you use for the purpose of control and calibration on the equipment?

A. Yes, essentially that's right.

Q. When you say you get your standards from so and so, you don't mean you are subscribing to a code of ethics or anything of that sort, you mean that you are buying a compound which contains a known percentage and concentration of the drug you are interested in?

A. That's correct.

Q. And, therefore, when, in Exhibit 4 on page 2, there is reference to the materials supplied in the kit, and perhaps I could show you it. On page 2, Mr. Cimbura, Materials Supplied, includes a list of things starting I-labelled Digoxin and then sets out digoxin standards lettered A through F and of varying concentrations starting at .5, 1.0 nanograms, 2.0 nanograms, 3.0 nanograms, 4.0 nanograms, 6.0 nanograms per millilitre. Those are, if I understand it, six different jars, tubes, containers, what you will, full of a compound with those respective concentrations





DD 14

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of digoxin, are they not?

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A. These are what, sir?

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Q. Those are five - six known  
stated concentrations of digoxin?

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A. That's right.

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Q. Yes. And whether you use the  
ones that come up with the Beckman kit or <sup>by</sup> your

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digoxin compounds with those known or other known

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concentrations in them elsewhere, does that make any  
difference?

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A. It may make some technical  
difference from a point of view --

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THE COMMISSIONER: Just a moment,  
Mr. Cimbura.

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MR. OLAH: I am sorry, Mr. Commissioner,  
but because of the feedback from the microphones I am  
told by people sitting in the back of the courtroom  
they are having trouble hearing. I am wondering  
whether anything can be done to accommodate those  
people?

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THE COMMISSIONER: Have you got some  
technical solution for this?

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MR. OLAH: I don't know, they were  
asking me whether anything can be done. There is that  
problem with the noise emanating from the microphones  
and I am just relaying the message that was conveyed  
to me.



DM.jc  
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THE COMMISSIONER: We might do better without microphones at all.

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MR. LAMEK: Well, maybe we can labour on a little bit, is there still feedback? I was conscious of it at an earlier stage.

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THE COMMISSIONER: Can we worry about that between now and next Tuesday?

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MR. LAMEK: Yes, we are certainly the wrong group to bring a technical problem of that kind to.

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THE COMMISSIONER: Well, all right, we will see what we can do and it may mean something drastic. Yes, all right, you were talking about standards.

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MR. LAMEK: Q. We were talking about standards and you were about to say that it may make some technical difference at some point in the procedure, would you finish that thought, Mr. Cimbura?

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A. The point I was alluding to, I mentioned previously that the standards have been prepared in saline and also the variations in quantities and standards applied by the Beckman <sup>quantities?</sup> manufacturer you know, they are very small manufacturers (,) they are very small, just meant for one assay. Whereas the drug when I purchased it, or when I obtained it

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from the manufacturer I might obtain a large quantity of the drug so I can use it for more manipulations, technical manipulations and so on.

Q. When you say you changed your standards, you don't mean you adopted a new moral code or anything of that sort?

A. No.

Q. All you mean is that instead of using the standard that came with this kit you either acquired or in fact prepared your own standard?

A. That is correct, yes.

MR. MANNING: Excuse me, Mr. Commissioner, if I might and I am respectful of your remarks when I was cross-examining this witness, but I fail to see any difference between the kind of cross-examination that I was conducting and the examination that Mr. Lamek is conducting, that he is conducting right now with respect to this particular issue of standards?

THE COMMISSIONER: He is explaining what standards are.

MR. MANNING: Well, if he failed to do that at the outset when he has called this witness and the other counsel in their cross-examination ---

THE COMMISSIONER: We are doing this because we would like to understand it.





EE.3

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MR. MANNING: I understand that, sir.

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THE COMMISSIONER: If there is some problem as to what he has done if you want to come back you can come back, but in this particular case, as I understand it what Mr. Lamek is trying to do is to make it clear just what the word "standards" mean.

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MR. MANNING: That is exactly what I was driving at as well, sir.

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THE COMMISSIONER: That part I find is perfectly appropriate, that is not examination for discovery, that is just trying to understand his evidence.

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MR. MANNING: His evidence and going further in order to clarify certain matters and to put on the record some matters which have not yet been gone into, I can understand it, but is there a difference, sir, in the role that you will allow, and perhaps we should have this matter determined at the outset of this hearing, that Mr. Lamek can play and the role that you see myself or other counsel playing?

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THE COMMISSIONER: The answer to that is no, two letters, NO.

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MR. MANNING: I fail to see the distinction then between the area I was going into



EE.4

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and the area Mr. Lamek was now going into.

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THE COMMISSIONER: All right, thank you. If you would go ahead, Mr. Lamek.

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MR. LAMEK: Thank you, Mr. Commissioner.

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Q Mr. Cimbura, in the course of your evidence yesterday you were cross-examined by Mr. Ortved and you referred to certain studies that you had performed at the Centre when you studied the, you said the extent of the elevation in blood levels of digoxin after the death of children who had been on digoxin therapy and then apparently had died of natural causes.

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With respect to those studies, Mr. Cimbura, when were they performed? Have I sufficiently identified the studies I am trying to direct your mind to?

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A. Yes, you have. What was that final question?

Q When were they performed?

A. I don't have the exact time. In my mind, it could be obtained, it is available. As I recollect it it started some time after March, 1981 and went on for a period of time, I think some went on even quite recently still. I would have to get all that together, there were quite a few specimens







EE.5

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from quite a few babies received in 1981, and there were some later on with regard to other studies that were, however, could be used for the same purpose as the first one.

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Q. Were the children from whom these samples were obtained children other than those with which this Commission is concerned?

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A. Oh, yes, certainly, yes, these were children that had died after 1981.

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Q. I think you said in your evidence yesterday 34 children in the study group?

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A. 34 as I recollect it that had received digoxin, that's right.

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Q. And in respect of those children, did you have available ante mortem digoxin levels for blood?

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A. For analysis, no.

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Q. And you performed analyses on the ante mortem blood samples that were supplied, did you?

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A. The ante mortem samples were not available to me.

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Q. Were not available to you?

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A. No.

Q. Do you have recorded levels from ante mortem samples made available to you?







EE.6

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A. I have tried to obtain them. I don't believe I was successful in many instances.

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Q. And therefore what you obtained was post mortem blood from these children?

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A. That's correct, post mortem blood and other tissues.

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Q. And what was the source from which the post mortem blood was taken?

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A. It was taken either from the heart or sagittal sinus, and in some instances from different areas of the body and in some instances from abdominal cavity.

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Q. With respect to the post mortem samples, did you sample them by the RIA technique, or did you first, or at any stage, go through the HPLC screening separation technique prior to RIA analysis?

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A. By the HPLC, if I did HPLC it would be after the RIA as opposed to before. But to answer your question this was research work as far as I was concerned and as I recollect it in some cases I have used HPLC but in the majority of the cases only the RIA.

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Q. I think you told us that the highest post mortem blood level you found was 12.4





EE.7

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nanograms per millilitre?

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A. That was one of the 34 and

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that was the highest, that's right.

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Q. Was that a sample of heart blood?

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A. That was a sample of heart blood,

that's right.

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Q. But you do not know what the

8

ante mortem level had been?

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A. I don't have that information,

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that's right.

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Q. Was it the purpose of this study

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to try to determine the multiplier effect, the

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elevation effect after death that might occur in

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children who had been taking digoxin in life?

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A. The major intent of the study

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which started, as I said, just after 1981, was to

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determine the extent of the therapeutic levels in

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post mortem blood, you know, how far can they go to,

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because there was relatively very little information

anyway on the subject.

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Q. Would it not have been rather

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important to know where they started in terms of an

ante mortem level?

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A. Yes, it would be useful. Indeed

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there was some, however, there is literature and there

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EE.8

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are studies in the literature that have studied that aspect as far as the multiplying factor, as you call it.

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Q. I think you said yesterday that

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the one child who did have that 12.4 nanograms per millilitre of post mortem heart blood had last received a dose of digoxin 2-1/2 hours before its death?

7

A. That's right.

8

Q. And what is the significance of

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that piece of information?

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A. My information is that the child

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received that last dose by intramuscular injection

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and the administration of the drug by intramuscular

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injection, the level of concentration in the blood

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will, so to speak, peak or become, begin low and peak

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or reach its highest concentration in the blood at

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approximately and following that will decline so that

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by about 4 hours and after it will be what is referred

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to as a ~~study~~ <sup>steady</sup> state level, and then there will be a

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very slow decrease for the next let's say 24 hours

20

after that.

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The significance, the reason why I

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brought this up is that since in this child the dose

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was injected 2-1/2 hours prior to death, the level

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may have been still higher than it would have been

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EE.9

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at the <sup>steady</sup> study stage. I should say the level could  
have been still higher than it would have been at  
the <sup>steady</sup> study stage.

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Q. At 3, 4 or 5 hours lapse between  
the dose and death?

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A. That's right.

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evidence as to extraction yesterday that emerged in  
your cross-examination by Mr. Scott. Do I understand  
from what you were saying to Mr. Scott that the  
purpose of the extraction process when you are  
preparing a sample for RIA, the purpose of the  
extraction process is to refine or purify the sample —  
to get rid of the blood components that you are not  
interested in testing, is that a fair way of putting  
it?

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A. Yes, that is essentially one  
of the purposes of it, yes. Perhaps — it is an important  
purpose, that's right, yes.

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Q. But in the process as I under-  
stood you, you wanted to be sure that you haven't lost  
the very thing that you want to test for and measure,  
the digoxin itself?

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A. That's right.

Q. You don't want to throw the baby





EE.10

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out with the bath water, is what we are really saying.

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So you had what Mr. Scott referred to as a recovery

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rate which he was anxious to determine and it was

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to make sure either that in the extraction process

6

*you*  
~~to~~ find out how much of the digoxin you actually had

7

salvaged in the refined part, or the other side of

8

that coin how much you had lost in the process?

9

A. That's correct.

10

Q. And I understood you yesterday

11

to be talking in terms of recovery rates and talking

12

about how much you had lost, and the Commission<sup>er</sup> was

13

a little bit concerned that Mr. Scott thought it

14

meant how much you *managed* ~~meant~~ to salvage; it is really the

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same thing, isn't it, just measured from different

16

sides?

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A. I think you put it very well, it

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is the other side of the coin, actually what you

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determine is how much you have left after the

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extraction and from it infer how much you have left,

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that's right.

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FF/EMT/ak

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Q. Yes. Now as I recall your evidence I think you told us that your average recovery rate in this extraction process, preparing samples for RIA analysis of digoxin, was about 85%?

A. As I recall it, and I said I would get the detailed study --

Q. You would bring details later?

A. Yes.

Q. As Mr. Scott requested. That is to say after the extraction process 85% of the digoxin that was in the original sample is in your refined or purified sample?

A. That is right.

Q. Is that right?

A. That is right.

Q. Or the same thing, 15% has remained with the stuff that you made the extraction from?

A. That is right.

Q. Now can there be a recovery rate calculation or determination in the absence of an extraction process? Can you have one without the other?

It is a rather simple-minded question





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but I don't understand that possibility.

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A. Well, it is usually -  
extraction in toxicological work is a very common  
process. It is applied to just about any drug  
analyses.

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I suppose you could ~~use~~<sup>lose</sup> a drug  
through some other processes. You could lose drugs  
through some other manipulations and processes that go  
on in addition to the extraction process.

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Q. You might want to establish  
a recovery rate with respect to those other processes.

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A. You may wish to establish an  
overall recovery rate following, you know, the  
whole process which would take all manipulations into  
account.

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Q. Mr. Cimbura, in your opinion  
in preparation of a sample for RIA analysis of  
digoxin is the extraction process or extraction  
process of the kind that you described, is that an  
appropriate step to take in sample preparation?

A. Well, I believe it is appropriate,  
yes.

Q. Is it a necessary step to take  
in terms of refinement of result?

A. I am not in a position to say







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whether it is a necessary step because I haven't  
done enough evaluation to compare it with other  
means of RIA analyses.

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However, and again the differences  
must be considered that I am analyzing tissues of  
various sorts, and blood, whole blood, as opposed  
to, let's say, a much cleaner sample of serum or  
plasma that may be in the hospital, so that from  
th~~at~~ point of view I think extraction is appropriate.  
Whether it is necessary, I would have to do research  
work to determine that. I believe it is a useful  
process and an appropriate process and that is why  
we are using it.

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Q. Perhaps necessary is not an  
entirely satisfactory word.

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May I put it this way, Mr. Cimbura:  
you referred on a number of occasions during the  
course of the past few days to your being satisfied  
as to the accuracy of your test results and analytical  
measurements as opposed to a question of interpretation.

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Does the extraction process which you  
have described enhance the confidence that you have  
in the accuracy of your results because if it doesn't,  
why do you do it?

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A. Well, it does to some degree, yes.





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FF4

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Q. And when we are recording  
matters --

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A. Particularly when one deals with,  
you know, very bad tissue, and so on.

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Q. Yes.

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MR. STRATHY: Deals with what?

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THE WITNESS: When one deals with  
decomposed tissue and these were all considerations  
that did cross my mind and that I considered before  
deciding on the approach of our analysis.

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MR. LAMEK: Q. Now, Mr. Scott took  
you into another area after that - I'm sorry,  
Mr. Commissioner. Did you have in mind taking a  
short break?

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THE COMMISSIONER: Well, if we have  
a reasonable chance of finishing fairly soon we  
will wait it out, but if not --

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MR. LAMEK: I may be 10 or 15 minutes.

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THE COMMISSIONER: I would think if  
I were to put it to a vote we would let you go on  
for 10 or 15 minutes. Perhaps I am wrong.

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MR. LAMEK: It puts me under  
considerable pressure to finish in that time.

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THE COMMISSIONER: Well, what about  
taking 10 minutes then?

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---Short recess.





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---Upon resuming.

MR. LAMEK: Q. All right,  
Mr. Cimbura, we are heading for the last round-up.

Now after Mr. Scott had taken you  
through the business yesterday of extraction *and*  
recovery rates, he took you to something else which  
we had not discussed in your evidence in chief and  
that was the question of correction, and again let  
me tell you what I understood the evidence to be and if  
I got it wrong you had better put it right for me  
and for everybody. Certainly for me.

It was suggested to you that having  
produced a recovery rate of less than 100% (that is  
to say having acknowledged that the extraction  
process has lost a bit of the digoxin that was in  
the original sample) the results that you get on  
assaying the refined sample that comes out of that  
extraction process *are* ~~is~~ going to reflect something  
less than the full amount of digoxin in the original  
sample. And that therefore to reflect exactly what  
was in the original sample the reading on the  
refined sample should be adjusted to compensate  
for what has been lost in extraction.

Is that the purpose of the correction  
that was suggested to you?







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FF6

A. That would be a purpose of the correction if it was used, yes.

Q. Okay. Now I understand you said it wasn't used in your lab in any event.

A. As far as my recollection right now, and I promised to go through it, but as a general - as I recall it was not used, yes.

Q. Now again let me be clear. It was suggested to you that if, for example, in the course of extraction your recovery of the digoxin had only been to the extent of 50%, and assuming for the moment you ~~don't~~ <sup>would</sup> continue to work with an extraction process that allowed you to recover only 50%, if you only got 50% and assayed the resulting extracted sample, in order to get a reading of the level in the whole original sample, you would have had to multiply your eventual reading by 2. Is that fair?

A. Yes.

Q. If you were doing that, that way of making the adjustment?

A. That is right.

Q. Of compensating for the loss. Now your average recovery rate you say is about 85%. And I take it you established that by something





1  
2 like the use of standards again? You put through  
3 a known quantity in your original sample?

4 A. That is right. To the original  
5 sample and then after the extraction determining  
6 how much is left.

7 Q. Yes. Obviously you can't do it  
8 on a sample that is there for analysis, a sample  
9 taken from a body, because you don't know what is there  
10 in the first place. That is what you are trying to  
find out.

11 A. That is right.

12 Q. So you have to determine your  
13 recovery rate with a sample containing a known  
14 quantity of digoxin, don't you?

15 A. That is correct, yes. A so-called  
16 spiked specimen.

17 Q. A spiked specimen?

18 A. Yes.

19 Q. Now your average recovery rate  
20 was 85%. If you do not make a correction in your  
21 final reading to compensate for that loss of 15%,  
22 and if you take no other measures to compensate for  
23 that loss, would it follow that the readings you  
record are understated as levels in the original  
sample?

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A. Yes. If that was the only factor present.

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Q. If that was the only --

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A. The only factor present, yes.

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Q. In other words, if you started out with a sample that contained 10 nanograms per millilitre, you lost 15% (1½ of those nanograms in the extraction process) and you recorded 8.5 nanograms in the refined sample.

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A. Yes.

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Q. You correct by taking account of the fact you had lost 15% and making a mathematical adjustment to your reading? That would be one <sup>way</sup> of doing it?

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A. That is right.

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Q. Do you adopt some other technique for compensating for that lost digoxin in the extraction process?

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A. With respect to the digoxin analyses by RIA, with respect to the digoxin analyses, no, we have not corrected for this one factor that is involved.

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Q. Have you taken any other compensating procedure to account for the loss in extraction?

A. As I have said yesterday I want





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to go, you know, through our detailed experimental  
work to be able to answer this with absolute  
certainty.

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Q. Do you have a recollection,  
a general recollection?

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A. Yes, I have a recollection  
that we have not, but I would like to go through my  
experimental notes.

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Q. Of course, and you should, and  
you will have that opportunity.

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If your recollection is correct that  
you have in no way compensated for the loss which you  
know you experienced in the extraction process  
does it follow, Mr. Cimbura, that all your RIA  
analysis levels are understated in terms of the  
concentration of digoxin that existed in the original  
sample?

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A. Well, it could be understated  
because there are other factors involved.

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Q. Right. What are the other  
factors?

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A. There are factors of precision,  
for example, variations, you know, in the many  
manipulations with the resultant plus or minus degree  
of variation from, let us say, the true result. These







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are quite recognized variances due to the very many  
processes --

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Q. Yes.

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A. -- that this matter has to be  
taken through before it reaches the end.

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Q. Yes.

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A. Based on this one factor alone,  
yes, the results would be lower, would be expected  
to be lower.

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Q. Now in that context I was  
puzzled by an answer that you gave to Mr. Scott  
yesterday, and I don't know whether you still have  
with you in the witness box a copy of the transcript  
of yesterday's evidence, Mr. Cimbura. Do you have  
that with you?

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If you do, I would ask you to please  
leave that out of your briefcase because we need it  
when you go.

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A. Thank you. I meant to clarify  
it if it was for my own use or not for my own use.

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Q. At page 206, Mr. Cimbura,  
please. There is intense competition for copies at  
the moment and I am afraid we need all the copies  
we can get.

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At line 13 Mr. Scott had been asking





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you about the recovery rate, and he said:

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"So that the recovery rate is critical  
because it is the gauge by which you  
measure whether your ultimate reading  
bears any relation to reality?"

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And you said:

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"Yes, from the sense that, of course,  
if you lost a considerable amount then  
your readings would be much smaller  
than they should be in the original  
material."

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That is what we have just explained.

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And then Mr. Scott, in four words,  
confused me. He said "Exactly. And vice versa?",  
and you said "That is right".

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Now "And vice versa" is what puzzles  
me.

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THE COMMISSIONER: If you gained a  
considerable amount?

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MR. LAMEK: That is exactly my  
puzzlement, Mr. Chairman. Let's be clear because  
Mr. Scott is I am sure very careful with his words.  
You do have to watch every one.

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THE WITNESS: Can you give me the  
page again, sir?





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MR. LAMEK: Page 206. "So that  
the recovery rate is critical..." do you have that?

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THE WITNESS: I don't have a line 30.

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MR. LAMEK: Q. Line 13.

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A. Oh, I'm sorry, line 13.

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Q. "So that the recovery rate is  
critical because it is the gauge by  
which you measure whether your  
ultimate reading bears any relation  
to reality?

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A. Yes, from the sense that, of  
course, if you lost a considerable  
amount then your readings would be  
much smaller than they should be in  
the original material.

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Q. Exactly. And vice versa.

17

A. That is right."

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Now what does vice versa mean, Mr. Cimbura?  
What did you understand that question to me?

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You can't recover more than 100% of  
the original material, can you, in the extraction  
process.

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THE COMMISSIONER: I wouldn't fuss  
too much about it. We will ask Mr. Scott what he  
means.

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MR. LAMEK: Q. Well, let me clarify  
what I think the situation is, Mr. Cimbura.

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In the extraction process, if anything, as  
I understand it, you may fail to draw out all of  
the digoxin in the original sample?

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A. That is right.

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Q. But you are never going to end  
up, are you, with more digoxin in the refined sample  
than you had in the original?

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A. No, you cannot, physically you  
cannot.

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Q. That is right, and therefore  
if any correction is to be made or if you were  
making corrections to compensate for a loss incurred  
in the extraction, it could only be a calculation  
or a correction that would increase the actual reading  
to compensate for the loss; never one to decrease  
the actual reading to compensate for a gain?

A. That is for that one factor,  
that is right.

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A. For that one factor, that's right.

Q. That's right. In other words, a correction could only be upwards, not downwards?

A. That's right.

Q. And on the basis merely of recovery rate and extraction loss, you can only lose material producing an understated reading, you can never gain material producing an overstated reading, is that right?

A. Well, you can never gain material.

Q. Yes, and thereby produce an overstated reading. You can't have an overstated reading because you picked up material in the extraction process?

A. Unless your reading is false.

Q. Yes.

A. That is the only way it could happen.

Q. Sure, of course.

THE COMMISSIONER: We will give Mr. Scott equal time next week.

MR. LAMEK: Well, we can. I would love to hear what he thought he meant by that.





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Q. Okay, just a couple of matters arising out of a couple of points today, Mr. Cimbura. We have heard in the course of today when you were first approached by the police in March, 1981 to assist in their investigation of matters at Sick Children's Hospital your first response was that you and your facility had no expertise, didn't have procedures available and they should try somewhere else?

A. If there was somewhere else available, that's right.

Q. Did you make any suggestions as to where they might try? Did you know of any other place that might have the facilities and expertise?

A. There may have been, I'm not sure whether there are at this stage. I know that I have reviewed my mind for possible sources, reviewed what I know about agencies in, you know, the United States and so on and my knowledge of their experience and I'm not sure whether I discussed that with the police, no, I cannot recall.

Q. You would be thinking of forensic agencies and centres such as your own, I take it?

A. That's right, yes.







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Q. In the course of evaluating the RIA procedure for digoxin and working out and establishing the procedure that would be followed in your lab when you finally agreed to take the assignment on, you were aware, I take it, that at the Hospital for Sick Children they performed RIA assays for digoxin?

A. I was aware that they performed it on the specimens of serum or plasma.

Q. Yes.

A. And I believe I had information that they weren't, at least as I recall it and again this is a long time ago, that they were unable to analyze the tissues and the various other specimens that were produced. I may be wrong, this is my recollection going back two years.

Q. In considering and developing a procedure for your own lab, whether it be for liquid or blood or tissue assay, did you ever request assistance from the people at the Hospital for Sick Children with respect to their procedures? Did you seek information or advice from them?

A. I sought information with respect to co-operation and obtaining specimens for my research.

Q. Was that after you had established







GG 4

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and developed a procedure?

A. I don't recall that I have asked for information. I was approached for information by the Hospital for Sick Children but I don't recall whether I had initiated that.

Q. All right. Now, could we look briefly at Exhibit 4, which is the material from the Beckman people, the suppliers of the kits which you used in your RIA procedure. I think you told Mr. Strathy first of all this morning when he asked you about cross-reactivity with certain other drugs which may be administered along with digoxin. I think you told him that with respect to spironolactone, did you not say you separated that out by HPLC in your lab?

A. That's correct, sir.

Q. Now, as I look at page, whatever it is, it's the last page of Exhibit 4 where the drugs are listed, that is one of the listed drugs which is acknowledged by the manufacturers of the kit, the suppliers of the kit to have a cross-reactivity with their kit, is that fair?

A. That's correct.

Q. But it is also one of those very three end ones which you described as having very little cross-reactivity?





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GG 5

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A. That's correct.

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Q. Do you separate out by HPLC any of the other drugs listed in Exhibit 4 as being cross-reactive with the components of this kit?

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A. Yes, whatever drugs for which I could obtain standards, as I recall it, were used.

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Q. Are you able to recall which those are?

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A. I believe it was lanatoside C.

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Q. That's the first one on the left-hand column, yes. We know that digoxigenin is one of those metabolites, is it not?

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A. That's right, yes. I believe this was the one, yes, that we also separated on HPLC.

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Q. What about acetyl-digoxin?

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A. Acetyl-digoxin I believe I was unable to obtain a standard. I am not sure whether this drug is used in Canada or not.

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THE COMMISSIONER: I am sorry, you're not sure what?

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THE WITNESS: Whether the drug is medicinally used in Canada.

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THE COMMISSIONER: No, but the question was whether you separated it out.

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THE WITNESS: Yes, no.

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GG 7

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Q

~~Testosterone?~~

A

~~No.~~

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Q.

Progesterone?

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A.

No.

4

Q.

Are those not hormones?

5

A.

Pardon me?

6

Q.

Are those not hormones?

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A.

Yes.

8

Q.

And, therefore, are endogenous,  
are they not?

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A.

I am not sure whether they are  
endogenous.

10

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Q.

Certainly they can be  
administered?

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A.

That's right.

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Q.

Could you tell me what the  
numbers mean in the column headed Ratio Percent?

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What is the significance of those because we've got  
three with what look like substantial numbers and  
then decreasing down to less than 0.1 from 2.2.

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A.

Yes, 100 percent - if it was,  
just to illustrate to your question.

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Q.

Yes.

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A.

If it was 100 percent cross-  
reactivity it would be as reactive as digoxin itself.

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Q.

I see. It would be a perfect  
fit on the antibody, would it?

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GG 6

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THE COMMISSIONER: You may not have

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been there.

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THE WITNESS: No, I did not, sir,

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because I wasn't able to obtain a standard.

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MR. LAMEK: Mr. Cimbura said he

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couldn't get a standard, so therefore, he couldn't

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calibrate the machine to select that particular drug

9

but he's not sure whether it's medicinally used in

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Q. What about lanatoside B, Mr.

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Cimbura?

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A. I don't believe we have done

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that as well.

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Q. Digitoxin?

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A. Yes, we have done that, yes.

16

Q. That's separated out in HPLC?

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A. Yes.

18

Q. Lanatoside A?

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A. I don't believe so.

20

Q. Digitoxigenin?

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A. Yes, I believe so.

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Q. Ouabain?

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A. I believe so.

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Q. Testosterone?

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A. No, we haven't done that, no.





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GG 8

A. Yes. If it was - the lesser the number the more of the drug you would require to produce equivalent reading for digoxin on the assay.

Q. I see.

MR. MARSHALL: I am sorry, the smaller the number?

THE WITNESS: The smaller the number given in the table the more of that particular drug you would require to cross-react with the digoxin assay.

MR. LAMEK: Q. Well, if I understand you correctly, once we get down to the fourth drug in the left column, lanatoside B, which has a ratio percent stated of 2.2, from that point down the list to the end, do I understand you to be saying you would need substantial quantities of that drug present in the sample for it to be a serious competitor with digoxin for sites on the antibodies?

A. Yes, you would need more of it. For example, with digitoxin, which is the fifth on the list, you could get a measure by dividing .6 into 100, whatever it would turn out to be, that would be the amount you would need, more than digoxin, to give the same reaction.

Q. Now, this is the Beckman list of



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cross-reactive drugs?

A. That's right.

Q. Can you tell me whether other suppliers of digoxin assay kits similarly list the drugs to which their antibodies are cross-reactive?

A. I don't recollect reading through other manufacturers.

Q. All right. There is one other thing on that page that does interest me, Mr. Cimbura. At the bottom of it there is a table on the left-hand column, Amount of Digoxin Added, Amount of Digoxin Recovered, but immediately above that there is a paragraph headed "Recovery Studies". I want you to look at the last sentence of that, not because I understand the sentence or even do I ask you to explain it:

"The intercept of the regression line was used as the estimate of the endogenous digoxin value for the serum sample."

A. I am sorry, could you give me the page?

Q. Yes, it's immediately below the table that we were just looking at and it is merely the use of the expression "endogenous digoxin" that







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puzzles me. Does that mean what on its face it appears to mean that there is endogenous digoxin or do you understand it, in your much more expert reading of this than mine, to mean something else?

A. Well, I'm not particularly familiar with some of the terminology used here, such as the intercept of the regression line was used, I'm not, in my own experience, familiar with that.

Q. I can assure you in my own experience I'm not familiar with it either. It is just that --

A. The spiking.

Q. -- the combination of words "the endogenous digoxin".

A. That's right, at the beginning they referred to spiking a patient serum sample. Usually this term I am familiar with and is usually referred to by adding known amounts of digoxin to a preparation that does not contain digoxin.

Q. Well, I have heard of a similar meaning given to spiking in other contexts, Mr. Cimbura.

A. That's right, yes.

Q. But you have no explanation for the use of the language "endogenous digoxin". I am taking it entirely out of context, I understand, but







GG 11

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you can't help me with that?

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A. Not in addition to what I have already said.

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Q. And what you have already said is that to your knowledge there is no endogenous digoxin, no bodily manufactured digoxin?

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A. Digoxin as such.  
Q. As such. Just one other thing if I may about this Beckman kit. You referred to it in the course of Mr. Manning's cross-examination as a double antibody system. Can you tell me please what that means?

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A. Yes, this particular set of reagents contains a second antibody which was designed for the purpose of facilitating the physical separation of the complex that I have referred to before when we were discussing the RIA, the complex between the antigen and the antibody and the second antibody facilitates that and introduces to it some additional specificity and provides, in my view, a more precise analysis for digoxin.

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Q. So, having formed these complexes or complices, or whatever the plural of complex may be, of antibody and clustered digoxin and radioactive digoxin, you then had to separate them out, as you told





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us yesterday?

A. That's right.

Q. And it is in that second phase, the separation out, that the second antibody comes into the act?

A. That's right, yes.

Q. Right. Was that one of the bases upon which you selected the Beckman kit as the one of choice for your lab?

A. This was one of them, that's right.

Q. I understand that in other kits or in other RIA procedures <sup>for</sup> of digoxin, that separation may be done by charcoal?

A. By other means including charcoal, that's right.

Q. Do you have any opinion as to the relative desirability of one separation as opposed to the other one, the relative accuracy of one as opposed to the other?

A. I haven't done a study of that. One would have to compare or do an experiment by studying one side by side and I haven't done that, no.

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Q. Even without such side-by-side studies the presence of this method of separation as in this kit is one of the things that moved you towards Beckman?

A. Yes, I felt this is of beneficial value to the assay, that's right.

MR. LAMEK: Mr. Cimbura, you have been very kind, thank you very much.

MR. MANNING: I wondered while we are still on the topic of Exhibit 4 if I could ask Mr. Cimbura one or two questions arising directly out of what Mr. Lamek has asked?

THE COMMISSIONER: Yes.

FURTHER CROSS-EXAMINATION BY MR. MANNING:

Q. Mr. Cimbura, if you would take your attention back to Exhibit No. 4 to the third last paragraph on the page under the heading of "Recovery study", sir, Mr. Lamek asked you about the phrase "endogenous digoxin value"?

A. Yes, I remember that.

Q. Do you have that in front of you?

A. Yes, I have it now, that's fine.

Q. All right, under the sub heading of "Amount of digoxin added", we find a number of figures listed in a column on the left-hand side, do







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you see that, sir, there is a table there?

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A. The table below the paragraph

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that you mentioned?

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Q. That's correct.

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A. Yes.

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Q. And there are two headings, one

says "Amount of digoxin added" and the other says

8

"Amount of digoxin recovered".

9

A. That's right.

10

Q. And the fourth item in the left-

11

hand column, the figure is 4.26.

12

A. That's right.

13

Q. And that is the amount of digoxin

added, and the amount of digoxin recovered is 4.35?

14

A. That's right.

15

Q. Showing an increase of 102%?

16

A. That's right.

17

Q. Does that suggest to you, sir,

18

that perhaps one can increase the amount of digoxin

19

by reason of the body's manufacture of its own digoxin,

20

and that is why the manufacturers of this test, sir,

21

used the phrase "endogenous digoxin value"?

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A. It suggests to me, sir, that

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because of analytical variation the recovery was more  
than was added in.

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Q Do you understand the word  
"endogenous" to mean that the substance is manufactured  
within the body itself?

A That's right, is produced within  
the body itself.

Q And there are many bodily  
substances manufactured within the body itself, are  
there not?

A Many substances, that's right.

Q For example, the body manufactures  
its own morphinelike substances, correct, called  
endorphins?

A Apparently, yes, as far as I  
have read.

Q And so that it might be capable  
of manufacturing its own digoxin?

A Well, I haven't seen any  
published work where this was determined in humans.

MR. MANNING: No other questions.

THE COMMISSIONER: Mr. Lamek?

MR. LAMEK: Nothing more, thank you,  
Mr. Commissioner.

THE COMMISSIONER: Have you some  
comment? Thank you, Mr. Cimbura.

Have you some comment?





HH.4

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2 MR. LAMEK: I have only two things,  
3 Mr. Commissioner, if I may. Having confidently  
4 suggested on Tuesday that we would by today have  
5 dealt with at least two and perhaps three witnesses,  
6 and having said that we hoped to have Dr. Seccombe  
7 here today, obviously those plans went awry. The  
8 proposal has been to have Dr. Mirkin here on Tuesday  
9 and that may still occur, I need to speak to him, and  
10 have Dr. Seccombe here on Wednesday with the  
11 expectation he may be required to stay over on  
12 Thursday as well. Dr. Mirkin if he gives evidence  
13 on Tuesday will not be here for more than that day  
14 and therefore the probability would be that he can  
15 return to give evidence to be cross-examined at a  
16 later stage. It may be more desirable to defer his  
17 appearance until he can be here for a sufficient block  
18 of time to have cross-examination. In that case it  
19 may be that Drs. Ellis and Soldin from the Hospital,  
20 the Biochemistry Department, will be here on Tuesday,  
21 but I will advise counsel of that tomorrow.

22 The second thing if I may is, when  
23 I attempted to have the Statement of Prima Facie Facts  
24 marked as an exhibit on Tuesday you may remember  
25 there was a slight murmur of discontent with it. It  
was your pronouncement as I recall it, sir, that







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objections, comments and allegations of wrongdoing and anything of that sort were to reach us by the beginning of the sitting next week. Could I ask counsel, or those of you that intend to make any such written allegations of shortcomings by Monday so that they may be considered before we begin our hearing on Tuesday.

THE COMMISSIONER: All right. Yes, Mr. Manning?

MR. MANNING: Mr. Commissioner, may I ask when we may expect to receive a copy of the material that has already been filed?

THE COMMISSIONER: We have had one from Mr. Scott, has that been distributed?

MR. LAMEK: No.

THE COMMISSIONER: Is anybody else filing anything?

MR. BOGART: It is not that I am filing anything, sir, I am interested that all the material that was filed by counsel was to be distributed to other counsel.

THE COMMISSIONER: That was my understanding too, we are clear on the first one, that was Mr. Scott. Has any other been filed today?

MR. LAMEK: We had earlier received







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something from Miss Kately's firm and I don't know whether she intends to add anything more to it and we have something from Mr. Scott.

THE COMMISSIONER: If anyone has any objection to his or her material being distributed?

MS. KATELY: No.

THE COMMISSIONER: If no one has any objections to his or her objections being distributed to everybody, that is except the press. As soon as we can get out the Scott objections we will distribute them out and as soon as the others arrive if they haven't already been distributed by the authors maybe we can distribute them or at least make them available.

MR. LAMEK: May I take up that suggestion, Mr. Commissioner. If anyone else proposes to let us have comments by Monday perhaps they could send comments to all other counsel as well.

THE COMMISSIONER: That certainly would help and get it there faster.

Mr. Marshall.

MR. MARSHALL: If it doesn't arrive until Tuesday it will still be received?

THE COMMISSIONER: Oh, it will be received but the difficulty is we may well find ourselves





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distributing the original Statement of Facts without the benefit of your corrections if you don't get it to us until Tuesday.

MR. MARSHALL: I will see the press gets a copy of it.

THE COMMISSIONER: We will try and get the original in the hands of the press before you do, the race is to the swiftest.

MS. GOODMAN: We asked for summaries of witnesses to be prepared if at all possible and I am wondering if Mr. Lamek can advise us for any of the witnesses next week, we will have summaries before the witnesses appear?

THE COMMISSIONER: Mr. Lamek, can you help us with that?

MR. LAMEK: Only to this extent, Mr. Commissioner, it may be Miss Cronk will be leading the evidence of Dr. Ellis, I am very good at talking Miss Cronk into doing these things, Dr. Ellis and Dr. Soldin if they will be giving evidence next week and doing something.

THE COMMISSIONER: Have they not given evidence in the preliminary?

MR. LAMEK: One of them did, but then with respect to particular findings rather than as to the methodology.





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In the case of Dr. Seccombe, I will be seeing him but briefly again before he appears as a witness, to the extent that I am able to give any kind of outline of what he will say I will try to do it but I can't promise it will be very helpful.

THE COMMISSIONER: That is all we can ask. Yes, Miss Kitley?

MS. KITELY: If I can make one comment, sir, about the comments your Lordship made to Mr. Manning?

THE COMMISSIONER: Yes.

MS. KITELY: The concern I have, sir, is that the comments that you made to Mr. Manning with respect caused some difficulty in preparing for the witnesses. As I understood your comments, and I may have misunderstood them, you were indicating to him that he ought not to use a question unless he had some information that this standard was, for example, incorrect. That is awfully like the reverse onus that we started with in the agreed statement.

THE COMMISSIONER: I am not talking about onus, I am talking about time and that is really what my concern is. If we are ever going to get an answer we cannot go in too deeply. Now I don't mean this to be taken that you can't do a little fishing,







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but just don't do it too much, that is all I am asking.

MS. KITELY: Well, I appreciate that. The difficulty I have is that some of us have limited resources, we don't have the experts that either Commission Counsel or the Hospital quite frankly has. We have to use this to get information.

THE COMMISSIONER: Can I just put it this way. I would think any witnesses that the Commission brings forth to the extent of their time, to the extent that they are here and available, it may be somebody brought in from some place outside the city, to the extent that they are here, they surely will be happy to see you and you can discuss it ahead of time. All I am asking and you must understand, Miss Kiteley, all I am asking is that I don't want you to go into the whole process merely in the thought or the hope of something, and I am somewhat concerned about what your interest is in finding out the procedure. Maybe there is something more than I grasped, and I am talking about the Nurses' interest now at the moment. What is the interest of the Nurses' Association in finding out the procedure other than the interest that we all have?





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MS. KITELY: The procedure goes to the cause of death and the Nurses have as much interest in it as do anyone.

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THE COMMISSIONER: I am just asking you really to be reasonable, that's all, and you don't find that an unreasonable suggestion?

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MS. KITELY: No, in fact I have some reasonable suggestions which I hope will carry that out.

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THE COMMISSIONER: All right.

MS. KITELY: The difficulty that we experienced I think with Mr. Cimbura being two full days and setting us back in fact six days, is we didn't have an opportunity to speak with him. I think your suggestion about Mr. Manning having an opportunity to speak with him is delightful, and if that could be something that could be done for all of us, subject of course to the witnesses availability, I think it would speed things up enormously. For example, Dr. Soldin I think has been in the courtroom for the better part of two days. If he were available during the recesses and at lunch time I think we would all be further ahead.

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THE COMMISSIONER: What have I done here, is it Pandora's box?





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MR. MANNING: If I might. The initial problem is what is the Inquiry all about? In my respectful submission the Inquiry is to ascertain the facts and find out, and certainly no one has a greater interest in finding out what happened to those babies as best as possible than my clients and Mr. Tobias' clients and Mr. Shanahan's clients, the parents, no one. So we don't want to wait any longer, we don't want to wait around.

THE COMMISSIONER: I am not suggesting that.

MR. MANNING: But you cannot with the greatest of respect find out whether what was done was done correctly unless you know what was done and then compare it to what other people have done. Mr. Cimbura has attempted to give us through Mr. Lamek an outline of what he did. I found that, with the greatest of respect, lacking in certain detail, I still don't know the exact procedures he followed. Certainly if that had been brought out by Mr. Lamek and I was covering the same area for no reason whatsoever and fishing around, Mr. Commissioner, you are quite right in telling me don't go any further. I still cannot see any distinction between the area I was cross-examining and what Mr. Lamek did in







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so-called re-examination and I only use those terms because those are the terms that lawyers are familiar with in a courtroom setting.

THE COMMISSIONER: We will do our best to see that you get any information that you want. All I am trying to do and I think you understand what I am trying to do.

MR. MANNING: I certainly do.

THE COMMISSIONER: I understand you are an experienced Counsel and you know the difference, if this were a trial all of that sort of questioning that you are on and perhaps what Mr. Lamek was on would have been done before we got to it.

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MR. MANNING: I certainly do.

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THE COMMISSIONER: And you understand, you are an experienced counsel and you know the difference. If this were a trial all of that sort of questioning that you were on and perhaps a great deal of what Mr. Lamek was on would have been done before we got to it.

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We have seen a demonstration already how long it is going to take because everybody has a different view of what is important --

MR. MANNING: Of course.

THE COMMISSIONER: -- with respect to the evidence. You can't really say that Mr. Lamek didn't bring out the things that he thought were important for our purposes.

I am happy to have you bring out anything that you think is likely to cast a gloss, if you like, upon the evidence that has been given before, but I would like you, and I would like Miss Kitley and I would like anyone else who has an opportunity, and I think this opportunity has been made available - Mr. Marshall has already tendered his services in this respect - to do what you can of investigation beforehand so that we don't have to do this inquiry within the Inquiry itself.





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MR. MANNING: Except Miss Kitley has properly pointed out we are going to run into another problem because we are going to have a mini Commission outside of this Court Room.

THE COMMISSIONER: Well, that is all right. That is all right. And if what you discover is worthwhile examining upon, you will then examine upon it.

This man is coming back so that there is no problem as far as he is concerned. You can go into it at some later time if there is something. I am hoping that all of your questions will be resolved and you will be happy with what has happened, but if you are not, I would be the first, I would like to know. I would like to know if there is something wrong.

MR. MANNING: Well then I certainly intend between now and the next opportunity with Mr. Cimbura, to find out exactly --

THE COMMISSIONER: All right.

MR. MANNING: And similarly with respect to the prospective witnesses.

THE COMMISSIONER: All right, Mr. Manning. You know what my problem is.

Yes, Mr. Olah?





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MR. OLAH: I'm sorry, Mr. Commissioner.  
I think Mr. Manning and Miss Kitely are expressing  
concerns we all have. We have two concerns.

Firstly, we don't know what information  
is going to be adduced, what evidence is going to be  
adduced from the prospective witnesses because in  
some areas they didn't testify at the preliminary  
Inquiry and therefore we cannot prepare. That is  
number one problem.

I would expect that Commission Counsel  
has notes of anticipated evidence he expects to  
adduce, and at many preliminary inquiries I have  
done that kind of material is provided in advance  
to facilitate cross-examination.

I would suggest that we all would be  
expedited and the matter could be moved along very  
smoothly if we were given some outline of the  
prospective evidence. That is the first suggestion  
I have.

Secondly, we are labouring  
under the problem that if we don't have access to --

THE COMMISSIONER: That is quite a  
different problem, you understand, from the one we  
are discussing. That is a problem whether the  
evidence is going to be made available to you







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beforehand, and that Mr. Lamek has already offered to do, where it is available.

What I am concerned about is not that.

MR. OLAH: I understand, sir.

THE COMMISSIONER: It is going into the whole procedure.

MR. OLAH: I understand. I was going to make a suggestion on that, and the suggestion is the other problem we are labouring under is the lack of expert evidence, and perhaps some informal setting could be arranged whereby counsel can gather with the expert witnesses and assess or find out something about the area that we are going to be facing, and perhaps some sort of informal arrangement can be made with Commission Counsel to do that.

I suspect by doing those two matters, we can expedite these proceedings substantially. But the main criteria is getting evidence up in advance so that we know where we are going so that we can prepare.

THE COMMISSIONER: Well, that we are endeavouring to do, and you realize, of course, it is impossible to do in some instances. Where we





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can, as I understand Mr. Lamek's undertaking, that  
is what he is going to do.

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MR. OLAH: Thank you very much, sir.

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THE COMMISSIONER: Anything else  
now before we rise then?

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Mr. Lamek, have you anything else?

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MR. LAMEK: I just wanted it to be  
clear, Mr. Commissioner, that the undertaking I have  
given goes to the first of Mr. Olah's suggestions,  
which in the light of the undertaking was frankly  
not necessary. Not to the second. I can't undertake  
that witnesses that I may be able to call are even  
going to be prepared to come here if they are going  
to be subjected to the kind of thing that is being  
talked about.

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And I don't mean subjected in any  
pejorative way. I can understand perfectly that  
people want information, but nevertheless if I say  
to someone from the United States or someone who has  
a busy schedule such as Mr. Cimbura, if I said, now,  
look, I would like you to come here not just for a  
day and a half to give evidence but also make yourself  
available and take people through your files, it  
would not greatly surprise me if he said find someone  
else.





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THE COMMISSIONER: Well --

MR. LAMEK: This is a real world;  
it is not the best of all possible worlds.

THE COMMISSIONER: All I think that  
is being asked is if a witness has the time and is  
willing you might put the suggestion to him but you  
are certainly not being directed to do that.

MR. LAMEK: Sure, but there can be  
no undertaking.

THE COMMISSIONER: If you want to  
see what you can do about that without driving the  
witness away in fear or in anger.

MR. BOGART: Well, sir, I am neither  
agreeing or disagreeing with Mr. Lamek's remarks,  
but I do think that those remarks enhance the  
importance of attempting to prepare a statement of  
the witness beforehand.

I think a large part of the difficulty  
of the past few days has simply been an attempt to  
try to understand what the witness is saying.

THE COMMISSIONER: There probably  
has never been an inquiry where there have been  
more statements by a witness available beforehand  
because we had the preliminary Inquiry in which  
many of these witnesses have given evidence; we have





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had the Government Inquiry where the results of many of the witnesses had been there. We have had all sorts of other things that are available so you can't say that you have had nothing to assist you in this matter.

MR. BOGART: No, no.

THE COMMISSIONER: We are trying to assist you.

MR. BOGART: And I appreciate that.

THE COMMISSIONER: We are going to do the best we can. I don't expect you to be happy but I do expect you to appreciate that we are doing the best we can to resolve your problems.

MR. BOGART: Yes, sir, and I appreciate that, but you recall Mr. Sopinka's initial request about statements.

THE COMMISSIONER: Yes.

MR. BOGART: It was if the witness had testified before and his evidence was to be of a different nature or was to depart in some significant measure from his testimony before, then we should have a statement.

If the witness had not testified before then we should have a statement. And I







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would submit, sir, that the evidence that Mr. Cimbura gave today is not the sort of evidence that he gave at the preliminary Inquiry.

The evidence he may give subsequently may relate to the evidence he gave at the preliminary Inquiry.

THE COMMISSIONER: We will do our best. That is all we can do. We will probably not be able to satisfy you but we may satisfy our own conscience.

Anything else now? By way of complaints. We don't expect any other comment. I if there is anything by way of complaint by all means let us have it.

All right. Nobody will complain I guess if we rise now until Tuesday at 10 o'clock.

---Whereupon the hearing adjourned at 4:30 p.m. until Tuesday, June 28th, 1983 at 10:00 a.m.







